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SPACE STATION INFECTIOUS DISEASE RISKS

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A Conference Report Sponsored By

Biomedical Laboratories Branch
Medical Sciences Division

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Lyndon B. Johnson Space Center
Houston, Texas

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MEMORANDUM

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FROM: SD4/Deputy Chief, Biomedical Laboratories Branch

SIGNATURE Duane L. Pierson

Duane L. Pierson, Ph.D.

SUBJ: Space Station Infectious Disease Risks Conference Report

The Biomedical Laboratories Branch of the Medical Sciences Division sponsored a conference to consider the infectious disease risks associated with living and working in the closed environment of the Space Station. The recommendations formulated during the conference have provided valuable guidance in the development of the diagnostic microbiology capability and the overall infectious disease prevention program for Space Station. We would like to express our appreciation to the distinguished panel members, other participants, and attendees for the success of the conference.

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SPACE STATION INFECTIOUS DISEASE RISKS

CONFERENCE REPORT

Sponsored by

Biomedical Laboratories Branch

Medical Sciences Division

Coordinated and Prepared by

Northrop Services, Inc.

Life Sciences Laboratories

National Aeronautics and Space Administration
Lyndon B. Johnson Space Center
Houston, Texas

October 1986

PREFACE

The Space Station represents the beginning of man's permanent presence in space. A major NASA programmatic goal is to ensure the health and safety of the crewmembers during the construction phase and occupation of the station. Because the Space Station Health Maintenance Facility will provide primary health care for this effort, its design and development must ensure that all health care needs are met. An inflight diagnostic microbiology capability will be an important aspect of the Health Maintenance Facility, and the Microbiology Laboratory of the Biomedical Laboratories Branch is responsible for its development.

Initially, the crewmembers will work and live in the closed, microgravity environment for 90 days with no immediate rescue capability. An unscheduled rescue would be expensive and require approximately 28 days. The Space Station will utilize a closed Environmental Control and Life Support System with limited capability for removing chemical and biological agents. In this system, respirable air and potable water will be recycled for crew consumption during Space Station occupancy. The unique properties of the microgravity environment must also be considered. On Earth, gravity is an important physical force in reducing aerosols and, thus, the spread of some infectious diseases. While large particulates and droplets containing microorganisms are removed from the air in minutes on Earth, these aerosols may remain suspended for hours in microgravity.

Physiological alterations resulting from microgravity, such as fluid shifts, bone demineralization, and cardiopulmonary deconditioning, have been well described. However, the effects of long-duration exposures to microgravity on microbial pathogenicity, transmission of infectious agents, and the immune system have not been determined.

The planned 90-day rotation of crewmembers and replenishment of supplies will contribute to alterations in the microbial flora of the crew and the Space Station environment. Life sciences investigations using biological specimens, as well as bioprocessing and material processing, will further impact the environmental microbial load.

The risks of infectious diseases have been considered throughout the history of the space program, and many preventive measures have contributed to the absence of serious infectious disease in crewmembers. Although the risk of infectious disease on board the Space Station cannot be eliminated, it can be minimized through design features and carefully implemented preventive medicine measures. Inevitably, infectious diseases will occur, but the impact of such diseases will be reduced by rapid and effective treatment. An appropriate diagnostic microbiology capability will facilitate a responsive therapeutic regimen. Consideration of these issues serves as the foundation for the conference proceedings that follow.

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TABLES

SECTION 1

INTRODUCTION

On October 29 and 30, 1985, the NASA/JSC Biomedical Laboratories Branch (SD4) sponsored a conference at the Lunar and Planetary Institute to address the impact of infectious diseases on the habitability of the Space Station. A panel of specialists, representing both the clinical and laboratory aspects of infectious disease, reviewed current policies and proposed microbiological requirements related to preventing infectious diseases from endangering crew health. During the two days of discussion, the panel defined issues critical to crew health and suggested approaches to the prevention and management of infectious disease. Each attendee was encouraged to voice personal views and participate fully in the panel discussion.

In particular, the panel members were responsible for four key tasks, summarized below:

(1) Identify the infectious diseases most likely to occur in the Space Station environment.

(2) Define the materials and methods needed in the Space Station Health Maintenance Facility (HMF) for the diagnosis and treatment of infectious diseases.

(3) Propose procedures and policies to minimize infectious disease occurrences in the Space Station.

(4) Recommend pre-Space Station studies related to microbiological infectious diseases.

To help panel members better understand the issues to be addressed, an initial presentation to the group by NASA specialists provided general information relating to infectious disease risks. For example, working in the Space Station environment will necessitate exposure to microgravity for a 90-day period, during which 6 to 12 individuals will be in close contact with each other in the enclosed environment. Personnel and equipment will be rotated, possibly providing suitable conditions for buildup of infectious agents. The specialists also informed the panel that, in the case of an emergency, a rescue would require 28 days.

Additional background information relating to the discussions was presented, including experience with infectious diseases in prior spaceflights. Extensive and careful medical and microbiological monitoring indicated infectious diseases to be a common problem during previous flight programs. Initially, this consisted of common infectious diseases such as acute respiratory and gastrointestinal illnesses (table 1-1). Because of their frequency, a preflight isolation period was instituted, and no further difficulty has occurred (table 1-2). Other infectious disease events included skin infections, presumed to be related to problems with space suit humidity and space suit cleaning.

Astronaut and environmental microbiological sampling revealed an exchange of microorganisms between astronauts and a quantitative increase in environmental contamination on some occasions.

The final subject presented to the panel related to immunological evaluations. Shuttle mission postflight studies have indicated immunological perturbations, most likely related to stress. How these alterations affect the immunological defense against infectious agents is unknown.

With this background information as a guide, the participants discussed each task issue. From the deliberations, the panel made recommendations on general requirements and responded to specific questions. At the conclusion of the conference, Dr. Robert B. Couch, Co-chairman, prepared a written summary of the panel's consensus on recommendations. This summary plus the minutes of the panel meetings form the foundation for the discussions in this report.

With regard to further discussion and development of plans and procedures, the panel agreed that any research or development should be considered as an operational need and recommended that a timetable be developed for conducting the research before final Space Station preparations.

The agenda for this conference is shown in section 2 of this report. A list of the panel participants is presented in section 3. Section 4 contains a summary of the discussions and recommendations for each of the four issues to which the panel was tasked to respond. The participants supplemented their comments at the conference with written commentaries, copies of which are included as appendix A of this report. Some of the materials supplied to the participants for review prior to the conference are shown in appendix B.

TABLE 1-1.- OCCURRENCE OF INFECTIOUS DISEASES PRIOR TO IMPLEMENTATION OF THE PREFLIGHT HEALTH STABILIZATION PROGRAM

Mission	Mission Phase	Number of Crewmen Involved	Illness	Comments
Apollo 7	Inflight	3	Upper Respiratory Infection	Influenza A, Hong Kong B, Streptococcus – Group A
Apollo 8	Pre- and Inflight	3	Gastroenteritis	Presumably viral
Apollo 9	Pre- and Postflight	3	Upper Respiratory Infection	Influenza B
Apollo 10	Preflight	2	Upper Respiratory Infection	Influenza
Apollo 11			Upper Respiratory Infection	
Apollo 12	Inflight	2	Skin Infection	Dermatitis, scattered staph-like pustules; *S. aureus* was abundant on crew and spacecraft postflight
Apollo 13	Pre- and Inflight	2	Urinary Tract Infection	*Pseudomonas aeruginosa* isolated from urine postflight

TABLE 1-2.- OCCURRENCE OF INFECTIOUS DISEASES AFTER IMPLEMENTATION OF THE PREFLIGHT HEALTH STABILIZATION PROGRAM

Mission	Mission Phase	Number of Crewmen Involved	Illness
Apollo 14			–
Apollo 15			–
Apollo 16			–
Apollo 17	Preflight	1	Skin Infection
Skylab 2			–
Skylab 3	Inflight	2	Skin Infection
Skylab 4	Inflight	2	Skin Infection
ASTP			–

SECTION 2

CONFERENCE AGENDA

INFECTIOUS DISEASE CONFERENCE
Lunar and Planetary Institute
Houston, TX, October 29-30, 1985

Time	Remarks	Speaker
October 29		
1:00 p.m.	Introduction	D.L. Pierson
1:15 p.m.	Welcome	J.P. Kerwin N.M. Cintron
1:30 p.m.	Space Station Overview	D.M. Germany
2:00 p.m.	Panel Responsibilities	R.B. Couch
2:15 p.m.	Anticipated Infectious Diseases in the Space Station Environment	Panel
3:15 p.m.	Break	
3:30 p.m.	Proposed Microbiological Support Plan	D.L. Pierson
4:00 p.m.	Discussion	Panel
5:00 p.m.	Summation	R.B. Couch
5:30 p.m.	Adjournment	
6:00 p.m.	Reception – Hilton, Nassau Bay	
October 30		
8:30 a.m.	Continental Breakfast at LPI	
9:00 a.m.	Vitek Technology	C.E. Stager
9:15 a.m.	Overview of Health Maintenance Facility	J.S. Logan
10:00 a.m.	Break	
10:15 a.m.	Recommendations for Pre-Space Station Microbiological Studies	Panel
11:15 a.m.	Open Forum	All
11:45 a.m.	Summation	R.B. Couch D.L. Pierson
12:00 noon	Adjournment	

SECTION 3

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Co-chairmen

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SECTION 4

ISSUES AND RECOMMENDATIONS

4.1 IDENTIFICATION OF INFECTIOUS DISEASES

Discussion

The panel's initial task was to identify the infectious diseases anticipated in the Space Station. As a guide for discussion on this topic, a list of possible infectious diseases and their associated pathogens was given to the panel for evaluation (see appendix B, table 1). In general, the panel participants concurred with the contents of this list, making only minor revisions. The suggestion was made that infectious diseases of the eye due to possible irritation or abrasion could be a major problem and should be added to the list. The pathogens of interest were *Chlamydia* and pneumococcus, as well as herpes simplex and adenovirus. The panel also recommended eliminating *Corynebacterium diphtheriae* from the upper respiratory infection pathogen list, because the potential risk of infection by this organism was considered negligible. The panel's revised list of possible infectious pathogens is included in table 4-1.

In identifying possible infectious diseases, many of the participants emphasized that eye infections as well as upper respiratory, gastrointestinal, urinary tract, skin, and systemic infections could occur in the Space Station environment and were items of concern. For example, while one would expect gastrointestinal infections to occur infrequently, they could be devastating by easily spreading to other crewmembers.

The unique skin problems created by working in space suits were also addressed. The environmental conditions created while working in a space suit for several hours are conducive to the development of superficial mycoses.

The panel approached identification of these infectious diseases in terms of areas of risks, concluding that the common risks associated with living in an urban U.S. environment are the primary ones encountered on prior flights (e.g., acute respiratory infections, acute gastroenteritis, and common skin infections previously discussed). Less common infectious agents prevalent in our society include such organisms as hepatitis viruses, *Chlamydia*, gonococcus, and Epstein-Barr (EB) virus. Possible unique exposures include infectious agents brought to the space crew by exposure to preflight personnel or to a foreign astronaut with an infectious agent not ordinarily seen in the United States.

Environmental exposures may arise from preflight or inflight contamination of food, water, or environmental surfaces and from contamination that might result from improper waste disposal. A variety of scientific experiments will be conducted on the Space Station involving plants, laboratory animals, and microorganisms, which could introduce infectious agents. In addition, accidents probably will occur, producing wounds that may become infected with microorganisms. Other considerations should include exposure from unexpected circumstances, such as the disruption of the Space Station Environmental Control and Life Support System (ECLSS), microbial mutation (resulting in increased virulence), or alteration of astronauts' host defenses.

Recommendations

The panel's recommendations to JSC in identifying infectious diseases can be summarized as follows:

- Include on the list of possible risks infectious diseases of the eye due to irritation or abrasions.
- Eliminate *Corynebacterium diphtheriae* from the list of upper respiratory tract pathogens.
- Recognize the important risks of upper respiratory tract, gastrointestinal tract, urinary tract, and skin infections.
- Assess potential risks according to area or means by which infection might occur.

4.2 MATERIALS AND METHODS FOR THE HEALTH MAINTENANCE FACILITY

Discussion

The second task of the panel was to define the materials and methods needed in the Space Station HMF for diagnosis and treatment of the infectious diseases described in section 4.1.

On this topic, the panel was asked to consider the following specific questions:

- Is there a need for inflight capability for the following microbial agents?
  (1) Viruses
  (2) Anaerobes
  (3) *Chlamydia*
  (4) Filamentous fungi
  (5) *Legionella*
  (6) *Mycoplasma*
  (7) Other aerobic and microaerophilic bacteria (those not listed in table 1, appendix B; e.g., *Campylobacter*)
  (8) Parasites

- Should microbial procedures be conducted in an enclosed workstation?
- What antibiotics should be included on board?
- What additional capabilities and equipment are needed?

Dr. Pierson provided a list of proposed HMF diagnostic capabilities (see appendix B, Inflight Capabilities), which served as the foundation for discussing microbiological diagnostic approaches needed in the Space Station. With few additions and deletions, the list reflected the diagnostic capability the panel thought appropriate for bacterial diseases. Additionally, the panel evaluated information describing the Vitek AutoMicrobic System (AMS).

With regard to viruses, the panel did not believe a tissue culture capability was necessary. This opinion was based on the expectation that a future capability for most viruses can be included without requiring tissue culture, eggs, or other living systems. As one panel member explained, by 1992 there should be a rapid viral diagnostic, dry technology for most of the viruses. Another panel member noted that during the past several years new technologies have arisen that give enormous promise for the future. These methodologies depend upon the use of DNA probes for the identification of microorganisms. The panel did suggest that NASA monitor the evolving DNA probe technology and consider incorporating these technologies for rapid identification of bacteria and viruses as they become available.

In considering the other specific agents, the panel advocated techniques for detection of *Chlamydia*, *Mycoplasma*, *Legionella*, and *Campylobacter*. Anaerobic capability could be limited to blood culture techniques. The panel agreed that a procedure for identifying fungi and parasites should be present, but presumed that current slide technology for wet and dry mounts would be sufficient for both.

The panel concurred with the adaptation of Vitek technology for identification of aerobic bacteria and yeast, and for the performance of Minimum Inhibitory Concentration (MIC) antibiotic susceptibility testing. Some of the advantages of the AMS were its cards' compactness, long shelf life, containment properties, and ease of use.

Because the Space Station will use a closed environmental control system with recirculating air, control of microbial agents released when conducting microbiological procedures in microgravity is extremely important. Such an environmental system has limited ability to remove potentially harmful microbiological agents. Thus, the panel stressed that all microbiological work must be performed in an enclosed workstation. Adequate decontamination procedures for all areas should also be developed.

The panel suggested a number of antimicrobials for treatment of various infectious diseases. A composite of some of the recommended agents and their spectra is shown in table 4-2. These recommendations were made with the stipulation that the therapeutic regimens be reviewed annually and modified to reflect advances in treatment of infectious diseases. If available, the panel recommended that both an oral and an intravenous preparation be included.

In terms of other new technologies or equipment, the requirement for digital color microscopy was listed as a high priority to permit examination of urine, blood cells, Gram stains, and microorganisms. It was noted that this technology would also be necessary for the study of filamentous fungi and parasites. A transmission capability for high fidelity viewing of diagnostic materials by experts on Earth was identified as an essential element of the inflight microbiology laboratory. The panel concluded that JSC should re-evaluate all diagnostic capabilities frequently.

Recommendations

The panel's recommendations to JSC for defining materials and methods for use in the HMF can be summarized as follows:

- Concurred with adaptation of Vitek technology for bacterial identification and determination of antibiotic susceptibilities.
- Recommended including capabilities for detection of *Chlamydia, Mycoplasma, Legionella*, and *Campylobacter*, but limiting anaerobic capability to blood cultures.
- Recommended identification of fungi and parasites, relying on wet and dry mount slides.
- Advised that tissue culture for viral propagation and identification was not required.
- Listed various antimicrobials (table 4-2) for treatment of infectious diseases.
- Stressed that all microbiological work must be performed in an enclosed workstation.
- Assigned high priority to digital color microscopy with transmission capability.
- Suggested close monitoring of DNA probe technologies.

4.3 PROCEDURES AND POLICIES TO MINIMIZE INFECTIOUS DISEASE

Discussion

The panel's third task was to establish preventive measures that would minimize the risk of infectious disease occurrences during a 90-day Space Station mission. Among the preventive measures to be considered were the adequacy of the 14-day quarantine period and preflight screening for venereal disease, as well as a comprehensive monitoring and vaccination program (see table 4-3). The participants also considered possible exposures to unusual infectious agents transmitted to the crew by foreign nationals involved in Space Station operation.

As a basis for these discussions, the panel evaluated the preflight health plan prepared by NASA and the materials included in appendix B of this report. The panel endorsed the plan, adding several agents to the list for preflight serological screening. Specifically, the panel recommended that preflight serological screening should be expanded to include the following:

a. Herpes simplex

b. *Mycoplasma pneumoniae*

c. Influenza

d. Systemic fungi

e. *Toxoplasma*

f. *Rickettsia*

g. *Chlamydia*

h. Human T-Lymphotropic Virus Type III (HTLV III)

In addition to the standard protocol of preflight physicals, the panel recommended that uretheral and genital cultures be taken. Also as a part of the preflight plan, it was advised that all vaccinations known to be safe and effective in preventing infectious diseases be administered to all astronauts who are candidates for the Space Station. Panel members agreed that such vaccinations represent one of the most effective measures available for preventing infectious diseases.

As to the question of quarantine duration, the panel generally agreed that the 14-day limit is adequate, but should be enforced strictly and in conjunction with a survey of family and community members who will be in contact with the crewmembers prior to duty. One panel member endorsed that, in addition to a complete review of known contacts with infectious diseases, the quarantine be extended to 30 days. He advised that this would not only identify any illness with short incubation periods such as common respiratory infections, but would include infections with longer incubations such as the adenoviruses. However, most of the panel members thought it unlikely that longer quarantine periods would result in significant additional protection from acquired viral illnesses.

Recommendations

A summary of the panel's recommendations to JSC for preventive measures follows:

- Adopt preflight health plan, Microbiology Support Plan for Space Station, JSC-32015, after necessary modifications are incorporated.

- Include venereal disease screening in preflight testing.
- Expand serological testing to include herpes simplex, *Mycoplasma pneumoniae*, influenza, systemic fungi, *Toxoplasma*, *Rickettsia*, *Chlamydia*, and HTLV-III.
- Require all safe and effective vaccinations.
- Adhere to a strict 14-day quarantine period with a survey of family and community members to identify contacts with infectious diseases during the 30 to 60 days prior to flight.
- Discourage crewmembers from eating shellfish during the four months preceding flight to help prevent hepatitis and vibrio infections.

4.4 PRE-SPACE STATION RESEARCH

Discussion

The panel's fourth and final task was to make recommendations for pre-Space Station studies related to infectious diseases. For these determinations, the participants discussed studies to be conducted prior to operation of the Space Station. These studies would include inflight assessment of the effects of microgravity and the spaceflight environment on host defenses and shedding of microorganisms, as well as their effects on growth characteristics of microorganisms and susceptibility to antimicrobials. The panel also considered a variety of techniques and equipment to be studied and tested in microgravity before incorporation into Space Station operation.

The question of compromised immunocompetence due to the effects of microgravity on host defenses was given the highest priority by the panel since all discussions and plans for prevention, diagnosis, and treatment of infectious diseases have assumed normal host defense mechanisms against infectious agents. If this is not a correct assumption, a full reconsideration must be made of the infectious disease risks from opportunistic organisms to a host with compromised immunocompetence.

Previous immunological studies presented at the meeting involved only pre- and postflight evaluation of crewmembers. These studies suggested that some decrease in immunocompetence may occur in the spaceflight environment, but the extent and degree of such immunological compromise were not known. Therefore, the panel emphasized that inflight studies to evaluate this phenomenon should be developed and implemented as soon as possible.

The panel further recommended that Shuttle flights should be used to conduct these evaluations and suggested such studies include an assessment of specific and non-specific defense mechanisms. This could include assessment of polymorphonuclear leukocyte function, macrophage function, and such items as intestinal motility and mucociliary clearance of respiratory passages. A relatively easy prospective clinical study would be to monitor shedding of herpes simplex virus and cytomegalovirus before, during, and after Shuttle flights.

The possibility of alterations in growth rates, colonial morphologies, and antimicrobial susceptibilities in spaceflight environment was also cited for study. Many unanswered questions concerning the behavior of bacteria in microgravity must be investigated to allow adequate planning for the microbiology laboratory capability in the Space Station. In conjunction with this, the panel recommended that the pharmacokinetics of the required therapeutics, including the absorption, distribution, and excretion of the drugs, be evaluated as well.

Since allergic reactions could impair crew performance, the panel supported research into the impact of these factors, recommending studies on allergic pneumonitis risks and appropriate research on the prevention, diagnosis, and treatment of diseases caused by filamentous fungi because of possible exposure in microgravity.

In the area of operation of various techniques and equipment, the panel deemed it essential that all methodologies being considered for diagnostic use be tested under actual operating conditions in space. For these studies, the panel advised that methodology for the HMF should be updated yearly, with further evaluations during Space Station occupancy as appropriate.

The participants further recommended that specialists in various disciplines be consulted regarding applicable Space Station infectious disease risks that are unique to their disciplines. Additional capabilities needed in the Space Station would be noted. These comments along with other information could be used to develop a set of algorithms for infectious risks to be incorporated into a manual for use by HMF personnel.

The panel included several additional recommendations. They advised that attention be given to the preparation, storage, and disposal of food before and after Space Station use. They also suggested a review of procedures for waste disposal and selection of water and air sources to minimize environmental risks from any of these areas. Finally, research on methods for decontamination of an enclosed workstation and the Space Station itself was suggested to avoid the potentially harmful buildup of contaminating microorganisms.

Recommendations

The panel's recommendations to JSC for pre-Space Station studies can be summarized as follows:

- Conduct inflight studies with Shuttle flights to evaluate effects of microgravity on immunocompetence.

- Direct studies to determine growth characteristics and antimicrobial susceptibility of microorganisms in microgravity.
- Utilize Shuttle flights and crew for pharmacokinetic studies on therapeutic agents.
- Develop algorithms of procedures and methodologies for an HMF manual to be evaluated and updated as appropriate.
- Test all selected techniques and equipment in actual microgravity flight conditions before incorporation into the Space Station HMF.
- Monitor procedures for food preparation, storage, and disposal, as well as waste disposal and air and water procurement.
- Conduct research on decontamination methods for enclosed workstations and the entire Space Station.

TABLE 4-1.- MICROBIOLOGY DIAGNOSTIC CAPABILITY FOR THE HMF

System Contingency	Specimen	Associated Diseases	Pathogens	Space Station Capability
Upper Respiratory Tract	Throat Nose	Pharyngitis Common cold Nasopharyngitis	*Streptococcus* Group A *Candida albicans* Respiratory viruses *Corynebacterium diptheriae* *Haemophilus influenzae* *Streptococcus pneumoniae* *Staphylococcus aureus*	*S. pyogenes* *S. pneumoniae* *C. albicans* *S. aureus* *H. influenzae*
	Middle Ear	Otitis media	*S. pneumoniae* *S. pyogenes* *S. aureus* *Pseudomonas aeruginosa*	All pathogens
	Sputum	Bacterial pneumoniae	*S. pneumoniae* *S. pyogenes* *S. aureus* *Enterobacteriaceae* *P aeruginosa* *Mycoplasma* spp. *Legjonella* spp.	All pathogens
Gastrointestinal Tract	Feces	Salmonellosis Shigellosis	*Salmonella* spp. *Shigella* spp. *Yersenia enterocolitica* *Campylobacter jejuni* *Escherichia coli* (enterotoxigenic)	*Salmonella* spp. *Shigella* spp.
Genitourinary Tract	Urine	Pyelonephritis Urethritis	*E. coli* *Klebsiella* spp. *Enterobacter* spp. *Proteus* spp.	All pathogens

TABLE 4-1.- Continued

System Contingency	Specimen	Associated Diseases	Pathogens	Space Station Capability
Genitourinary Tract (cont.)	Urine (cont.)		Other enteric bacilli and *P. aeruginosa* Enterococci *S. aureus* *C. albicans*	
	Vagina	Candidiasis	*Trichomonas vaginalis* *C. albicans* *Haemophilus vaginalis* Gonococcus Herpes simplex (Type II) *Enterobacteriaceae* *Streptococcus agalactiae* *S. aureus*	*T. vaginalis* *C. albicans* *S. aureus* *S. agalactiae*
Circulatory System	Blood	Bacteremia	*S. aureus* *S. epidermidis* *E. coli* *Klebsiella* spp. *Enterobacter* spp. *P. aeruginosa* *Proteus* spp. *Listeria monocytogenes* Anaerobic bacteria *C. albicans*	All pathogens except anaerobes
Central Nervous System	CSF	Bacterial Meningitis	*H. influenzae* *Neisseria meningitidis* *P. aeruginosa* *E. coli*, other Gram-negative bacilli	All pathogens

TABLE 4-1.- Concluded

System Contingency	Specimen	Associated Diseases	Pathogens	Space Station Capability
Central Nervous System (cont.)	CSF (cont.)		*S. aureus* *Streptococcus* spp. *Cryptococcus neoformans* *C. albicans* *L. monocytogenes*	
	Wound	Bacterial Cellulitis Gas Gangrene (myonecrosis)	*S. aureus* *S. pyogenes* Anaerobic bacteria *Enterobacteriaceae* *P. aeruginosa* Enterococci	*S. aureus* *S. pyogenes* *Enterobacteriaceae* *P. aeruginosa* Enterococci

TABLE 4-2.- ANTIMICROBIALS RECOMMENDED FOR THERAPEUTIC NEEDS IN THE SPACE STATION

Antibiotic	Type	Antimicrobial Spectrum
Acyclovir	Antiviral	Herpes simplex Type I and II Varicella-zoster Epstein-Barr Cytomegalovirus
Amantadine	Amantadine hydrochloride	Anti-Parkinson Antiviral - Prevention and treatment of respiratory illness caused by influenza A virus strain
Aminoglycoside Amikacin Gentamicin Kanamycin Tobramycin	Antibacterial	*Streptococcus* *Staphylococcus aureus* (some penicillinase-producing strains and methicillin-resistant strains) Gram-negative bacteria
Amphotericin B	Antifungal	Cutaneous and mucocutaneous mycotic infections caused by *Candida* species
Ceftriaxone	Antibacterial	Broad spectrum *Enterobacteriaceae* *Neisseria meningitidis* Beta-Lactamase positive *Haemophilus influenzae* and *Neisseria gonorrhoeae* Anaerobes
Cephalosporin 3rd generation	Antibacterial	Broad spectrum Gram-negative bacteria Gram-positive bacteria
Clindamycin	Antibacterial	Aerobic Gram-positive cocci bactria Anaerobic Gram-negative bacilli bacteria Anaerobic Gram-positive nonsporeforming bacilli bacteria Anaerobic and microaerophilic Gram-positive cocci bacteria
Erythromycin	Antibacterial	*Streptococcus pyogenes* Alpha-hemolytic Streptococci *Staphylococcus aureus* *Streptococcus pneumoniae* *Mycoplasma pneumoniae* *Haemophilus influenzae* *Corynebacterium diptheriae* *Listeria monocytogenes*
Imipenen	Antibacterial	Broad spectrum Gram-positive cocci bacteria Gram-negative bacilli bacteria Anaerobes

TABLE 4-2.- Continued

Antibiotic	Type	Antimicrobial Spectrum
Immune serum globulin	Gamma globulin	Broad spectrum Gram-positive bacteria Gram-negative bacteria
INH	Antibacterial	*Mycobacteria tuberculosis*
Ketaconazole	Antifungal	*Coccidioides* spp. *Histoplasma* spp. Chromomycosis Paracoccidioidomycosis *Candida* spp. Oral thrush
Metronidazole (IV)	Antibacterial	Anaerobic bacterial infections
Metronidazole (Oral)	Antiprotozoal	*Trichomonas* Amoebae Anaerobic bacteria
Micanazole cream	Antifungal	Common dermatophytes *Trichophyton rubrum* *Trichophyton mentagrophytes* *Epidermophyton floccosum* *Candida albicans* *Mallassezia furfur*
Nystatin suppositories	Antifungal	Vulvo-vaginal candidiasis
Opthalmic for herpes simplex	Antiviral	Herpes simplex
Penicillin-PNA-ase resistant Methicillin Nafcillin Oxacillin	Antibacterial	Penicillinase resistant *Staphylococcus* spp. *Pneumococcus* spp. *Streptococcus* spp.
Quinoline	Antiparasitic	*Plasmodium vivax* *Plasmodium malariae* *Plasmodium falciparum*
Rifampin	Antibacterial	Pulmonary tuberculosis *Neisseria meningitidis* nasopharyngeal carrier
Tetracycline	Antibacterial	Broad spectrum *Rickettsiae* *Mycoplasma pneumoniae* Agents of psittacosis and ornithosis

TABLE 4-2.- Concluded

Antibiotic	Type	Antimicrobial Spectrum
Tetracycline (cont.)	Antibacterial (cont.)	Broad spectrum Lymnphogranuloma venereum and granuloma inquinale Spirochetes Gram-negative bacteria Gram-positive bacteria
Topical for superficial mycoses	Antifungal	Yeasts Yeast-like fungi
Trimethoprim/ Sulfa	Antibacterial	*Enterobacteriaceae* – urinary tract infections *Haemophilus influenzae* Otidis *Streptococcus pneumoniae* Media *Shigella flexneri* *Shigella sonnei* *Pneumocytis carinii*
Vancomycin	Antibacterial	Gram-positive bacteria *Clostridium difficile*

TABLE 4-3.- PREFLIGHT PREVENTIVE MEASURES

Days Prior to Flight	Activity
90	Review of crewmembers' immune status to selected infectious agents, to include immunization with all safe and effective vaccines.
30	Flight physical (Crew Physician) includes complete clinical chemistry workup and check for tuberculosis.
	Microbiological analysis of crewmembers: Culture Ear Nose Throat Skin Urine Feces Sputum Venereal disease screen Blood (syphillis, AIDS) *Neisseria gonorrhoeae* screen Herpes simplex I and II screen Trichomonas examination
	Serum tested for the following: Invasive fungi Cytomegalovirus (CMV) *Toxoplasma* *Rickettsiae* *Legionella* *Chlamydiae* Herpes simplex I and II Influenzae Malarial antibodies Hepatitis A and B Respiratory Synctial Virus (RSV) Rotovirus
	Recommend 30-day preflight family member monitoring
14	Quarantine
	Microbiological analysis of crewmembers (same as F-30 except one additional throat swab will be taken for viral isolation).

TABLE 4-3.- Concluded

Days Prior to Flight	Activity
10	Flight physical (same as at F-30)
7	Microbiological analysis of crewmembers (same as F-14)
1	Flight physical (no laboratory work)
	Microbiological analysis of crewmembers (same as F-14)

Antibiotic susceptibilities will be determined for all potential bacteriological pathogens isolated during preflight microbiological evaluations.

Biotyping of selected isolates (e.g., phase typing of *Staphylococcus aureus*) will be conducted for epidemiological applications.

Preflight microbial monitoring of the Space Station environment (air, surfaces, water, and food) will be conducted to ensure a safe environment for crewmembers (see Microbiology Requirements and Specifications for the Space Station Document).

APPENDIX A

WRITTEN COMMENTARIES BY PANEL PARTICIPANTS

The following pages are copies of the individual reports submitted by panel participants. Further details and suggestions from the conference are included in these commentaries.

Chairman's Summary of NASA Workshop on
Infectious Diseases in Space Station
Robert B. Couch, M.D.

BACKGROUND

A panel of Infectious Disease and Microbiology specialists was convened for a one day workshop to discuss and consider crew health in space station with regard to infectious disease risks and approaches to prevention and management of infectious diseases.

An initial presentation to the committee by NASA specialists provided general information relating to infectious disease risks: space station will consist of exposure to zero gravity for a ninety day period of six to twelve individuals in close contact with each other. There will be a rotation of both personnel and equipment, but a circumstance for perpetuation of an environmental microorganism and human infectious disease transmission problem exists. Finally, the committee was informed that a rescue because of medical problems would require a 28 day period.

Additional background information relating to the discussions was the experience in prior space flights with regard to infectious diseases. Extensive and careful medical and microbe monitoring had shown infectious diseases to be a common problem in former flights. Initially, this consisted of common infectious diseases in our urban society such as acute respiratory and gastrointestinal illnesses. Because of the frequency of these, a preflight isolation period was instituted, and no further difficulty has occurred. The other infectious disease problem has been skin infection presumed to be related to problems with cleanliness and space suit humidity. Astronaut and environmental microbe sampling had revealed an exchange of microorganisms between astronauts so that they eventually developed a "common flora" and a quantitative increase in environmental contamination on some occasions.

The final information sought by the committee was information relating to immunological evaluations. It was revealed that studies have been limited to postflight, and these revealed a number of immunological perturbations presumed most likely to be reactions to stress.

PANEL RESPONSIBILITY

Responsibilities of the panel were as follows:

1. Identify the infectious diseases that could occur in the space station environment.

2. Define the materials and methods needed in the health maintenance facility for diagnosis and treatment of possible infectious diseases.

3. Propose procedures and policies to minimize infectious disease occurrences in space station.

4. Make recommendations for pre-space station microbiological-infectious disease related studies.

POTENTIAL INFECTIOUS DISEASES FOR SPACE STATION

A suggested outline for assessing infectious disease risks is as follows:

1. Common risks associated with exposures during normal living in an urban U.S. environment.

2. Possible unique risks from unique exposures

    person exposures:
        preflight personnel exposures
        astronauts from foreign countries

    environmental exposures
        food, water, environmental surfaces
        astronaut waste

    experiment exposures
        animals
        plants
        microorganisms

    accidents

3. Unanticipated exposures

    microbial mutation

    impaired host defenses

    disruption of space station environmental control

The common risks associated with normal living in an urban U.S. environment are primarily those encountered on prior flights. These include the acute respiratory infections, acute gastroenteritis and the common skin infections. Less common infections that are prevalent in our society include such organisms as hepatitis viruses, chlamydia, the gonococcus and EB virus. Possible unique exposures might be infectious agents brought to the space crew by exposure to preflight personnel or to an astronaut from a foreign country with an infectious disease not ordinarily seen in the U.S. Environmental exposures might arise from preflight or inflight contamination of food, water or environmental surfaces, and contamination that might result from improper astronaut waste disposal. A variety of scientific experiments will be conducted on space station that will involve plants, laboratory animals and microorganisms, some of which could produce human disease. In addition, accidents probably will occur, producing wounds that may become secondarily infected with microorganisms. Finally, considerations should include those of unanticipated exposure that might occur from such circumstances as the disruption of space station environmental control so that living habits are altered, microbial mutation as a result of normal flora exposure to hostile environments, and unanticipated alteration in host defense of the astronauts. The latter is of particular concern and will be separately addressed; this workshp proceded with the assumption that the astronauts would be normal with regard to host defenses against infectious diseases throughout the extraterrestrial experience.

MATERIALS AND METHODS FOR THE HEALTH MAINTENANCE FACILITY

The discussion on microbiologic diagnostic therapeutic capabilities for the health maintenance facility used as a format the proposed diagnostic capability provided by Dr. Pierson. A few additions and deletions from that list constituted the diagnostic capability thought appropriate by the workshop group for bacterial diseases. The group endorsed the plan for incorporating an automicrobic system into the health maintenance facility.

The following specific agents were separately considered:

Viruses - The consulting group did not believe a tissue culture capability would be required and did not recommend that this be incorporated into the facility. They do, however, recommend a close monitoring of diagnostic technology development for viruses using non-living systems with the expectation that a capability for most viruses can be included without requiring tissue culture eggs or other living systems.

Anaerobes - The review group did not recommend incorporation of capability for culturing anaerobic microorganisms.

Chlamydia - The group recommended chlamydia diagnostic capability be included, but recommended that this be restricted to systems not requiring tissue cultures

Mycoplasma - The committee recommended mycoplasma diagnostic capability be incorporated in the health maintenance facility.

Fungi - The committee recommended this capability be present but presumed that slide technology for wet and dry mounts would be sufficient.

Parasitology - The committee recommended this capability be included but believed that slide mounts for wet and dry capability would be sufficient.

Legionella - The committee strongly endorsed the incorporation of this diagnostic capability into the health maintenance facility.

The committee recommended that all microbial procedures be carried out in a glove box and that projection capability for accurate viewing of diagnostic results on earth be incorporated into the health maintenance facility. Finally, frequent reconsideration of the diagnostic capability should be made so that methods are current and incorporate capability for any potential exposures that might be introduced as a result of specific scientific experiments or flight by persons providing unique risks.

The following antibiotics, antifungals and antivirals are recommended for incorporation into the health maintenance facility:

Penicillin	an aminoglycoside	Ketaconazole	Acyclovir
Erythromycin	Vancomycin	Amphotericin B	Amantadine
Tetracycline	Imipinum	a topical fungal for	an opthalmic for
Trimethoprin/	Ceftrioxime	superficial mycoses	herpes simplex
Sulfa	a quinoline	Metronidizole	immune serum globulin

Where both an oral and an intravenous or intramuscuular preparation are available, both are recommended for inclusion. Discussion was not given to amount of drug, but it is suggested that sufficient medication should be available for 14 days of therapy for 2 individuals with each drug.

PROCEDURES AND POLICIES TO MINIMIZE INFECTIOUS DISEASE

The committee endorsed the preflight health plan prepared by Dr. Pierson; influenza, herpes simplex virus and mycoplasma pneumoniae were added to the preflight serologic testing. The blood and urine parameter testing was considered appropriate, but the committee strongly recommended that the quarantine period be extended from 14 to 30 days preflight. This would not only identify any illnesses with short incubation periods such as the common respiratory infections, but would include incubation periods of common infections with longer incubation periods such as mycoplasma pneumoniae and adenoviruses.

A system for monitoring infectious diseases in all family members of astronauts should be conducted during the 30 to 60 day period preceding flight by that individual. Finally, the quarantine period should be a strictly controlled period providing essentially no exposure to outside personnel.

The crew member microbial analysis list was deemed appropriate except that respiratory syncytial virus should be added and a nose wash and rectal swab should be added to the throat swab specimen currently obtained for viruses. In addition, preflight screening should include sexually transmitted diseases. Finally, the committee recommended that all vaccines for infectious agents that are known to be safe and effective for preventing an infectious disease be considered for administration to all astronauts who are candidates for space station duty since this represents one of the most effective preventive measures available for the infectious diseases.

RECOMMENDATIONS FOR PRE-SPACE STATION RESEARCH

The committee recommended the following research for consideration beginning in the immediate future in preparation for space station occupancy.

1. An assessment of immunocompetence of astronauts during space flight.
   The committee considered this research to be of the highest priority since all discussions and plans for prevention, diagnosis and treatment of infectious diseases assumed that occupants of space station would be normal with regard to host defense mechanisms against infectious agents. If this should not be a correct assumption, then a full reconsideration must be made of the infectious disease risk because of the extensive number and seriousness of infections that might occur with opportunistic organisms if astronauts are not immunocompetent. The committee recommended a specific consideration be given to obtaining these evaluations in the present shuttle flights and generally suggested they include an assessment of specific and non-specific defense mechanisms; this could include assessment of polymorphonuclear leukocyte function, macrophage function, and such items as intestinal motility and mucociliary clearance of the respiratory passages. A relatively easy prospective clinical study which could be implemented soon would be to monitor shedding of herpes simplex virus and cytomegalovirus before, during and after shuttle flight.

2. An assessment should be made of microbiologic methods in space with regard to growth of organisms, appearance of colonies and function of the vitech methodology.

3. Microbiologic methodology for the health maintenance facility should be specifically updated on a yearly basis, commencing now, with further evaluation of methods during space station occupancy as appropriate.

4. Research on methods for decontamination of the glove box for microbiology and the space station environment itself in order to avoid environmental build-up of otherwise innocuous microorganisms.

5. Give specific consideration to the preparation, storage and disposal of food before and after space station, procedures for waste disposal and sources of water and air to insure absence of an environmental risk to astronauts from any of these areas. The committee assumed that this would represent special considerations by appropriate specialists.

6. An assessment of the absorption, distribution and excretion of drugs, including antibiotics, should be made during current shuttle flights so that planning for space station will include the knowledge that pharmacokinetic behavior of antibiotic therapy will or will not conform to existing information.

7. The committee recommended consideration be given to allergic pneumonitis risk and appropriate research on prevention, diagnosis and treatment because of the possible exposure to filamentous fungi in a zero gravity environment.

8. The committee recommended a set of algorithms be developed for the infectious disease risks that can be incorporated into a manual for use by the person or persons responsible for health care of the astronauts in space station.

9. The committee recommended specialists in ophthalmology, dentistry and dermatology be separately consulted regarding the infectious disease risks that are unique to their discipline and might be applicable to space station. Additional capability may be required for the health maintenance facility.

FINAL COMMENTS

The workshop group developed a format for preparing for infectious disease problems in space station with the understanding that the task was that of health maintenance and not of research. We believe that the format provided can serve as a basis for developing more detailed information in specific areas discussed and can lead to effective preparation for this area of health maintenance by the time of space station occupancy. With regard to further discussion and development of the plans and procedure, the workshop committee believes very strongly that any research or development should be considered as an operational need and recommends that a tentative time table be developed for conducting the research in sufficient time to utilize the results in final preparations for space station.

SUMMARY OF THE INFECTIOUS DISEASES WORKSHOP HELD AT THE LUNAR AND PLANETARY INSTITUTE

James R. Davis, Ph.D.

The concerns expressed by the Infectious Disease panel can be divided into three areas: A) Prevention, B) Detection and C) Treatment.

A. Prevention was addressed relative to preflight quarantine, testing and immunization. The single greatest unknown and concern expressed was the immune competence of individuals exposed to relatively long-term microgravity. The other aspect of prevention discussed by the panel was inspace environmental concerns. This was not a principal responsibility of the Infectious Disease panel but obviously could have significant impact on the spectrum of infectious disease possibilities. The panel suggested that they or a similar group have input and review of the environmental control procedures as they relate to food, water, air and general public health or sanitation requirements.

B. Detection: The recommendations for detection can be summarized as follows:

1. Parasites and filamentous fungi can be adequately handled without culture providing a digital microscope with telemetry capability and materials for direct examination of specimens are available.

2. Anaerobic microbiology capability is not necessary except for certain specimens such as blood and spinal fluid. In these circumstances, the requirement is to be able to grow and determine whether the organism is a true anaerobe or not. Identification and susceptibility testing, not required.

3. Bacteria: The aerobic and microaerophilic bacteria of concern were generally defined as normal flora with two exceptions, Legionella and Campylobacter. The specific methods and techniques for culture of these microbes were not addressed but the concensus opinion was that direct

methods such as latex agglutination-type procedures for antigen detection as well as gene probes be applied whenever available and practical. When more classical techniques for culture and susceptibility are required, the Vitek Auto Microbic System (AMS) or some adaptation of this technology was the method of choice.

4. Viruses: limited virology capability recommended. This is intended to identify the more common viral infections. Non-cultural techniques recommended whenever possible.
5. Chlamydiae: direct detection methodologies preferred.
6. Mycoplasma: The availability of cultural techniques desirable for specific species, i.e., *M. pneumoniae*, *U. urealyticum*.

The techniques which will be required in this area need considerable development and testing before the space station is operational. The emphasis should be on a workable mix of established and anticipated technology such as gene probes.

C. Treatment: The treatment discussed was focused upon antibiotic modalities and did not include other considerations which will need to be defined at some stage. The concensus was that a certain number of spaces for antimicrobics must be designated. This would include considerations of how many cases of X disease must we anticipate, etc. While a list of antibiotics was made, I believe this is only appropriate as a guide to space requirements since by 1994 many of these drugs will be out-moded.

The panel also addressed specific areas where investigation and technical development were needed.

A series of studies to evaluate the immune status of man in space were discussed.

The specific recommendations are captured on the tape and I will not try to list them. There are many unanswered questions regarding the behavior of bacteria in microgravity which must be answered to allow adequate planning for the microbiology laboratory capability in the space station. Again, these specific recommendations are on the tape but they included such simple but absolutely critical questions as the growth rate of microbes in microgravity.

There are treatment questions of great significance which must be addressed that involve both the host and infectious agents. What are the effects of microgravity on adsorption and metabolism of antimicrobials in the host and what effects on microbial resistance are expected?

This brief narrative summary of the Infectious Disease panel discussions encompass in a general fashion all three of the basic charges of this group. Specific details are provided in the accompanying material. In addition, I believe this accompanying material can be made more complete upon review of the tape. I will be more than happy to review and to help edit a transcript of these proceedings.

James R. Davis, Ph.D.

OPEN QUESTIONS

1. Do we need an inflight capability for the following:

   A. Viruses: limited to the most common agents such as HSV and Influenza. Non-culture method whenever possible.

   B. Anaerobes: no, except blood and CSF. Should be no more than the ability to determine whether truly anaerobes or not.

   C. Chlamydiae: yes - direct detection methods only.

   D. Filamentous Fungi: direct mounts or stain capability with Telemeter of digital microscopy for definitive identification. May wish to culture and transport to earth for further examination.

   E. Legionella: yes, culture or direct examination methods if suitable.

   F. Mycoplasma: yes - limited to a few species.

   G. Other Aerobic and Microaerophilic Bacteria: yes - culture should include Campylobacter.

   H. Parasitology: yes - same as for filamentous fungi.

   I. Yeast: yes, culture.

2. Is the Quarantine Period appropriate?

   Fourteen day strict quarantine with complete review of known contacts with infectious diseases during the past 30 days.

3. Do we need a Venereal Disease Screening Preflight?

   Yes - complete and including AIDS.

4. Should crew be vaccinated against specific infectious disease agents?

   Yes, immunization status should be as complete as possible, including any anticipated exposures to international infectious diseases.

5. What antibiotics should be included onboard?

   The list developed by the panel is recorded on the tape, however the recommendation was to provide space and the precise antibiotics could be defined at a later time.

6. Should inflight surveillance be conducted?

   No, not of personnel.

ADDITIONAL COMMENTS

1. Specific and detailed algorithms for diagnosis and treatment of the expected infectious disease should be developed. These should include public health measures such as the wearing of masks, etc. The laboratory aspects of isolation, identification and susceptibility testing of potential pathogens should also be available.
2. The types of food to be eaten before a flight should be evaluated. For example, raw shell fish should not be eaten during the preflight quarantine period.
3. The monitoring of space craft and space station for mycobacteria should be considered.
4. Latex agglutination and other serologic procedures should be evaluated. The existing slide technology may need to be adapted to a closed system such as capillary pipettes.

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SCHOOL OF MEDICINE
DEPARTMENT OF INTERNAL MEDICINE

November 20, 1985

Duane L. Pierson
Deputy Chief, Biomedical
Laboratories Branch
Lyndon B. Johnson Space Center
Houston, Texas 77058

Dear Dr. Pierson:

Thank you for the opportunity to participate in the Infectious Disease Workshop in October, 1985. I found the discussions informative and worthwhile. Enclosed are comments and recommendations with regard to these discussions. These statements are organized as answers to the discussion questions on the last page of the handout entitled, "Proposed Microbiological Support Plan for Space Station." I somehow did not receive the format for the report. I will gladly fill out such a format if desired.

1. Do we need to define an inflight capability for the following microbial agents?

A. Viruses

Comment - Viruses have caused infections in preflight crew members, in crew members post flight and in backup crew members. (1) Viruses have also been isolated from personnel working with the crews. The post flight illnesses were due to infection and influenza A2, Hong Kong and Influenza B. Viral contacts were with rhinoviruses, herpesviruses, ECHO, adenovirus and Coxsackie virus. Thus, viral infections have been proven to occur during space flight.

Recognition of this likelihood has resulted in a plan for serologic testing to determine the crew members immune status prior to space flight. According to the information in Appendices I and 3 tests are to be performed for Hepatitis A and B, EB virus, mumps, rubella, rubeola, varicella zoster and CMV. Throat swabs are also to be cultured for influenza, parainfluenza, herpes simplex, adenovirus, coxsackie virus, rhinovirus and enterovirus.

Recommendations

1. On the basis of the above documentation and on the known transmissibility of viral infections, inflight viral diagnostic

2. Influenza is a potential cause for infection even in immunized individuals and because of 1) the potential for transiently debilitating illness and 2) the availability of amantadine, inflight diagnostic capability of this virus should be present for influenza. The standard method of culture is too cumbersome and too technically difficult to recommend. Serologies are also not useful as they afford retrospective diagnosis. Influenza virus can be identified by fluorescent antibody methodologies using monoclonal antibodies and this test, if it can be accomodated and performed appropriately should be available in the HMF.

3. Herpes simplex is also a potential cause for infection and because of 1) the availability of acyclovir and 2) the potential for transmission, fluorescent antibody testing with monoclonal antibodies should be available in the HMF. It is important to note that for inexperienced personnel, herpes simplex lesions may be incorrectly diagnosed leading to failure to treat with acyclovir or treatment with acyclovir when unnecessary. Since acyclovir may cause diarrhea, nausea or vomiting, albeit infrequently, unnecessary treatment should be avoided. <u>The fluorescent antibody test for H. simplex using monoclonal antibodies should be available in the HMF.</u>

4. Rotavirus infections are now recognized as occurring much more commonly in adults than previously considered. Although therapy does not exist for rotavirus infection, the fact that epidemic spread can occur and the potential for misuse of antibiotics due to incorrectly diagnosed gastroenteritis warrants the following:

   a) <u>testing of the crew for group A rotavirus infection with Rotazyme (Abbott Laboratories) prior to the quarantine period and</u>

   b) <u>Having the diagnostic test available in the HMF.</u>

5. <u>As was mentioned at the Conference ELISA and Western Blot testing for AIDS antibody should be performed in the preflight period.</u>

6. DNA methodologies are available for detecting CMV as well as other viruses. At present these are inpractical for the HMF, but because of rapid advances in this field, diagnostic kits requiring minimal technical expertise may be available in time for installation on space station. <u>Someone should be assigned to monitor this technology for potential use.</u>

B. Anaerobes

Comment - Anaerobes are unlikely to be important causes for infection in the space station. This fact coupled with their complexity as regards detection, their predictable antimicrobial sensititivies, and their favorable response to treatment with "safe" antibiotics (clindamycin, metronidazole) indicates that the HMF need not have inflight diagnostic capability.

C. Chlamydia

Comment - Chlamydial infections have not been found in previous missions. Thus, although these infections are common (C. trachomatis) this absence coupled with the brief period of incubation (3 days to 3 weeks) and the need for sexual transmission, somewhat unlikely in the space station environment, indicates that infection in space station personnel in unlikely. Moreover, the commonly used technique for identifying C. trachomatis elementary bodies with fluorescein conjugated monoclonal antibodies requires considerable expertise. I do not believe inflight diagnostic capability is adviseable for the above arguments. Chlamydia psittici causes a severe pneumonia. The uncommon nature of the infection, its brief 7-15 day incubation period and the need to culture the virus with its attendant risk are reasons for not having inflight diagnostic capability for C. psittici.

D. Filamentous Fungi

Comment - Infections with these fungi are highly unlikely in nonimmunocompromised hosts.

Recommendation - Inflight diagnostic capability is not needed for these fungi (Aspergillus, Zysomycetes, etc..

E. Legionella

Comment - This organism is an important cause of pneumonia. It is spread by the airborne route usually via infected aerosols with contaminated water being an important common source

Recommendation - Appropriate decontamination of water is critical. Since unrecognized aerosol spread is possible, and since Legionella spp. can be identified with fluorescent antibody techniques this test should be available in the HMF.

F. Parasitology

Comment - Acute parasitic infections with amebae, giardia, ascariasis, hookworm, etc., are unlikely in the absence of contaminated water or individuals harboring these organisms and therefore, inflight diagnostic capability is unnecessary.

Recommendation - Test for the presence of parasites in stools and for the presence of malarial antibodies in serum prior to the space flight.

II. Should microbiological procedures be carried out in a glove box?

Recommendation - A glove box will be necessary to carry out microbiological procedures for a number of reasons, Firstly, the threat of aerosol infection is probably unduly high due to the absence of gravity. Secondly, organisms like Shigella, Legionnaire's bacillus, etc can clearly cause infection in susceptible individuals if they escape and contaminate foods or water.

III. Is the quarantine period appropriate?

The 14 day quarantine period protects against most but not all viral infections. However, in view of the extensive preflight testing for the agents with longer incubation periods, i.e. Hepatitis A and B, EB virus, longer quarantine periods are unlikely to result in additional protection from acquired viral illness.

IV. Is the preflight venereal disease screening needed?

Comment - Among venereal infections syphilis, gonorrhea, AIDS and Herpes simplex are ones which might be present in a subclinical state.

Recommendation - Serologic tests for syphilis and AIDS should be performed prior to the flight. Similarly, vaginal and cervical cultures for gonorrhea should be performed as well as cultures of any male urethral exudates. A history of herpetic infection should also be sought.

V. What antibiotics should be included in the HMF?

Recommendation

1. Penicillin - (procaine and penicillin UK)
2. Erythromycin
3. Tetracycline
4. Trimethoprim - sulfa (oral)
5. Metronidazole (oral and parenteral)
6. Cefazolin
7. Ceftazidime
8. Ceftriaxone
9. Acyclovir
10. Amantadine
11. Ketoconazole
12. Nystatin suppositories
13. Miconazole cream
14. INH
15. Rifampin

VI. Should crew members be vaccinated against specific infectious diseases?

Recommendation - Current immunizations to include hepatitis B, influenza and pneumonia. Also when available varicella zoster should be given.

VII. What additional capabilities and equipment are needed?

Recommendation - A centrifuge would be of value in preparing specimens which require physical separation, i.e. sputum for TB, CSF, etc.

Lastly, many of the diagnostic techniques recommended at the meeting and which I have included in this report require considerable technical skill. I am sure you recognize this, but I wish to reemphasize the importance of human performance. Fluorescent tests in particular, are fraught with false positive and false negative results. Whoever is assigned to perform the myriad of laboratory procedures contemplated must be extremely well trained.

I hope that the above comments and recommendations are helpful.

Sincerely,

Elliot Goldstein, M.D.
Professor and Chief
Division of Infectious Diseases

Brigham and Women's Hospital
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Harvard Medical School
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November 7, 1985

Ms. Karen Gaiser
LSL - 37
Northrop Services, Inc.
PO Box 34416
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Dear Ms. Gaiser:

Thank you for all of the fine arrangements for the infectious disease workshop. I was delighted to be able to take part and learned a great deal about the progress that has taken place since I left the Space Science Board in 1973. Appended is my report. I have kept it brief, but shall be happy to add substantially to this if you so desire. Obviously, it is something in which I have a deep interest and shall be delighted to explore further if this is of interest to your company and to the Agency.

Enclosed also is my expense account.

With best wishes and appreciation to all,

Sincerely yours,

Edward H. Kass, M.D./jc

Edward H. Kass, M.D.

EHK:jc

enclosures

(Signed in Dr. Kass'absence to avoid delay.)

The plans for the proposed Space Station Health Facility are well-advanced. There will still need to be a great deal of discussion about the specific antimicrobial agents that should be carried aboard. The present prospectus with respect to the microbiological capability is sound and covers a wide and reasonable range of anticipated problems of an infectious nature.

My chief comment about these is the one that I made at the meeting. They are not meant to be critical of what has been proposed but are meant instead to look into newer capabilities that might be ready in time for the proposed liftoff.

The diagnostic approach to the cultivation and identification of bacteria has not changed, in its basic form, since the turn of the century. The use of nutrient agar, enriched in a variety of ways, complemented by microscopic examination and by specific fermentation reactions remains the core of microbiologic diagnosis. To this has been added special techniques requiring cell culture, for viruses and for certain of the more demanding bacteria such as Chlamydia. This is the present state-of-the-art and if one were to fly tomorrow this is the capability that is necessarily the only one that can be aboard.

However, during the past several years, new technologies have arisen that give enormous promise for the future. These technologies depend upon the use of DNA probes for the identification of microorganisms. Already, in a few trial instances, these have been shown to be sensitive and highly specific. They are rapid, precise, and in experienced hands give excellent results. The chief difficulty is that the technology has not been widely enough explored so that the battery of available DNA's for diagnostic purposes is exceedingly limited.

One of the most important roles that NASA has played has been the development of new technologies that have ultimately been of substantial benefit to society at large. In the microbiological area, one can cite the work of Moore et al. at Virginia Polytechnic Institute. These studies were funded by NASA at a time when relatively little was known about anaerobes, and the technology for rapid cultivation and identification of these organisms was in a primitive state. The group at VPI spend a number of years developing the technology and it is this technology that lies at the base of virtually all anaerobe work that goes on in medical laboratories throughout the world.

One can hope that something similar to this can be worked out in relation to DNA probes. In anticipation of a flight plan that requires hardening the plan within 4-5 years, it would still be possible to develop the following:

a. To prepare DNA from the wide range of bacteria that can reasonably be anticipated to become potential problems in space flight;

b. To prepare similar DNA probes for the variety of viruses and fastidious bacteria that would also be anticipated;

c. Develop a rapid and reproducible technology for the use of these probes for diagnostic purposes;

d. Such rapid approaches, based on a very large number of DNA probes, might encompass the development of pooling techniques such as has been used for the typing of pneumococci, with separation of the components of a given pool after identification of a positive within the pool;

e. Microorganisms could be pooled in relation to the relative probability of causing an infection in flight, thereby making the process maximally efficient.

In brief outline, this is the approach that might be taken. Laboratories that are competent in this area can be sub-contracted to produce the necessary probes. One central laboratory could be contracted to receive the probes, test them, work out the pools, test the pools both in laboratory and field conditions, and work out miniaturized instrumentation that would be dedicated to the DNA probe method.

These are entirely feasible objectives with a three year target for accumulation and testing of the material, if there is a determination to move ahead. I would recommend this approach highly as another example in which NASA may exert its leadership, this time in the medical field.

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Veterans Administration

In Reply Refer To:

November 1, 1985

Duane Pierson, Ph.D.
Biomedical Laboratories Branch
Medical Sciences Division
NASA Johnson Space Center
Houston, Texas 77058

Dear Duane:

I was pleased with the outcome of the Infectious Disease Conference sponsored by NASA this week. The Panel was expert, with diverse skills, and most of the important issues were addressed. I hope you will find our deliberations helpful as we head down the short time table for providing specifications for the microbiology/infectious diseases aspect of the Space Station Health Maintenance facility.

In my report, I will follow your suggested outline, and will emphasize items I feel to be most important rather than try to review all the discussion.

Identify Infectious Diseases to be expected in space.

1. Need to establish immunocompetency during space flight is of highest importance. The potential for exposure to very large microbial loads in space by the respiratory, GI and skin routes is very high because of the closed environment and past history of breakdowns in environmental control. Even very slight impairments in host resistance could become critical in determining susceptability of "normal" people to excessive microbial challenge. If abnormalities of host defenses are detected during space flight, then our list of potential pathogens is greatly expanded.

2. Your list of suspected common illnesses according to body site is very good, and I have only a few suggestions for additions:

a. Respiratory, including the eye. I would definitely add m. pneumoniae as a very likely pathogen - methods for rapid dx by FA are available, and ELISA techniques should be available soon.

Chalamydia have recently been implicated as the most common cause of pharyngitis in one study, and their potential for causing pneumonia and eye infections is well established. FA methods for rapid dx are commercially available.

Legionella is a very likely pathogen in this environment, even in normal people. The FA technique offers rapid and specific diagnosis with reasonable specificity and sensitivity.

Aspergillus because of the known heavy load in the closed environment is an important potential pathogen, particularly to produce disease by the allergic route. An alogorithm for suspecting and evaluating allergic pneumonitis needs to be written and probably would include such clues as atypical or "viral" pneumonia without isolation of bacterial pathogens, acute decrease in lung compliance and evidence for airflow obstruction, eosinophilia peripherally and particularly in respiratory secretions. A preponderance of lymphocytes in the respiratory secretions would also be suggestive.

Viral illnesses of the respiratory tract including influenza, adenoviruses and CMV need to be considered and included in the diagnostic potential because of the current and anticipated availability of antivirals.

b. Genitourinary Infections including venereal diseases need increased attention, in pre-screening cultures of the male urethra for chlamydia, G.C. and herpes and of the vagina for these plus trichomonas. Ability to diagnose venereal infections in space is necessary. Even if NASA were to prohibit sexual activity in space, I am not aware that any society has ever succeeded in such prohibitions.

c. Gastrointestinal Infections To your list, I would add clostridia difficle - a known environmental pathogen and occasional cause of diarrhea even in the absence of antimicrobial treatment. Cryptosporidiosis is another recently described enteric pathogen that could become a problem in the closed environment. Diagnosis is by acid/fast stain of the stool. Other common parasites including E. histolytica, giardia, strongyloides are potential problems and can be diagnosed by microscopic stool exam.

d. CNS I would certinaly include an LP kit, and methods for rapid diagnosis of CNS pathogens such as meningococci, H. Flu and pneumococcus. Identification of specific pathogens is important because of the need for prophylaxis.

e. Skin Past experience tells us that skin infections are common in space. Although initially a minor "irritation", over a long period these would be disabling. I would add pediculosis (lice & scabies) to the list of suspected pathogens which should be screened for, and for which therapy should be provided (Kwell shampoo).

f. Anaerobes These organisms will likely be important pathogens in abdominal infections; however, I would not go beyond the use of anaerobic blood culture media for their isolation and would not provide means for speciation of the anaerobes.

3. Diagnostic Needs

a. Rapid, specific pathogen oriented diagnostic techniques should be utilized as they become available (Group A Strep, capsulated CNS pathogens, legionella, etc.). Considerable effort should be given to providing the means for enzyme linked immuno assays (ELISA) for microbial antigens. It is likely that the dry film Kodak chemistry analyser could be adapted here.

b. I completely agree with Dr. Kass that NASA should encourage and support the development of Nucleic Acid probes for rapid identification of bacteria and viruses. These techniques will likely be "state of the Art" in 1992, and we should plan to incorporate these techniques as they become available.

c. The Vitek technology for bacterial speciation is attractive in concept, but a problem because of wt/volume consideration. I would encourage the company to develop for NASA a simple single plate for common pathogens, a syringe method of vacuum loading of the plate, and a method for reading the plates which utilizes a digital color camera on board with image reading and interpretations on the ground.

d. Digital Color Camera and Microscopy should be given high priority for inclusion in the diagnostic laboratory to permit exam of urine, blood cells and microbial colonies, stool parasites and gram stains.

4. Therapeutic Needs. It is likely that most of the antimicrobials we suggest for 1987 will be replaced in 1992 by superior agents. As a start however, I would include antimicrobials for

a. Staphylococci (Vancymycin and PCNase Resistant - Penicillin)
b. Gram Neg Bacilli (Aminoglycoside, 3rd Generation Cephalosporin)

c. New Broad Spectrum agents such as the isoquinolones.
d. Mycoplasmia, chlamydia, legionella (Erythromycin, Sulfa-trimethoprim)
e. Anaerobes - metronidazole, clindamycin, penicillin.
f. Parasites - metronidazole (oral and IV)
g. Fungi - Parenteral, Amphoterium B, oral ketoconazole
h. Other - Gammaglobulin should be made available

General: In choosing antimicrobials, those with longer half lives are most desirable. The possibility that many infections, although unlikely to occur, will likely involve many patients if they do occur, needs to be considered in calculating the number of courses of therapy to be provided on board.

5. Prevention.

a.) I agree with the group that there should be wide use of available and proven, effective immunizations. These include influenza, pneumococcus, H-influenza, meningoccocial, hepatitis, CMV and chickenpox for proven susceptables.

b.) The 14 day period of strict isolation before launch is appropriate if careful surveillence of family and other prior close contacts is practical.

c.) Eating of raw shellfish in the four months prior to flight should be discouraged to help prevent hepatitis and vibrio infections.

d.) Inflight culturing of the environment on current space flights should be expanded to include cultures for the atypical mycobacteria, legionella and acanthamoeba, Naegleria sp., since these could cause serious infections if present in large numbers.

e.) Very tight control of antibiotic use is necessary to prevent development of resistence.

6. Information Needed Before the Space Station is Established in 1992. High Priority for Current Shuttle Missions.

a. Effect of microgravity and space-flight environment on Host Defenses. This is the highest priority. The current studies which are limited to pre and post flight speciments are inadequate - emphasis needs to be given to inflight studies. Needed data includes:

b. Intensive in-flight monitoring for trivial infections which are often a clue to subtle defects in host defenses, i.e., Herpes Simplex virus. Incidence of cold sores and frequency of virus shedding in oro-pharyngeal secretions during flight as compared to ground.

Candida albicans oro-pharyngo-esophagitis, to be studied in-flight by exam and quantitation of microbial load.

Cytomeglovirus excretion in-flight. Probably also BK virus excretion in urine.

EB virus secretion in pharyngeal secretions in-flight.

ii. Pulmonary clearance studies - measure clearance rates for radiolabelled particles in man - and of infectious agents such as staphylococci in animals.

iii. Neutrophil function in flight including chemotaxis, phagocytosis, killing.

iv. Macrophage function, including lymphokine production, rates of phagocytosis and killing.

v. Cell mediated immunity at clinical level (skin tests), and in vitro including response to antigens as well as mitogens, and measurements of cytotxic and natural killer cell activity.

vi. Humoral immunity measured as antibody response to new antigens, and also compliment system activity.

b. Aerosol studies in flight to determine effect of weightlessness on survival and particle size of microbial aerosols.

c. Pharmacokinetic studies of absorption, distribution and excretion of antimicrobials (as well as other drugs).

d. Broader characterization of spacecraft endemic microflora to include atypical mycobacteria, acanthamoeba, legionella, changes in antimicrobial resistence patterns to potential pathogens (Staph aureus, enteric gram negative bacilli, etc.).

e. There is need for better integration of responsibilities for environmental control and monitoring with those responsible for the HMF at JSC. The current fragmentation of responsibilities inhibits acquisition of necessary information and will lead to unnecessary duplication of diagnostic equipment.

Finally, as I view the tremendous task ahead that needs to be accomplished in the next two years, it appears to me that the resources allocated to the microbiology needs at JSC are not adequate, particularly considering their divided commitment to servicing the current shuttle program as well as planning for the space stations.

I hope these comments will be of help to you.

Sincerely,

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Veterans
Administration

In Reply Refer To:

11/5/85

Northrop Services, Inc.
Ms. Karen Gaiser, LSL-37
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Dear Ms. Gaiser:

The following is my report following the Infectious Diseases Workshop for the Space Station Health Facility.

I will organize this based on the initial outline of responsibilities presented by Dr Couch as the meeting began: the infectious diseases and microorganisms expected, materials and methods needed to diagnose disease and identify organisms, procedures and policies needed to minimize, treat, and prevent infectious diseases, and recommendations for studies needed before final decisions can be made.

<u>1. Infectious diseases expected.</u> As became obvious during our early discussions, we have a major problem identifying the range of diseases to expect because of limited, preliminary information suggesting possible alterations in immune function during space flight. At this time we can't assume that space station inhabitants will have normal host defenses against organisms within their environment. Requirements for microbiological support are markedly different for immunocompetent, healthy adults, and for immunocompromised individuals. Moveover, require-

ments are dependent on the type of compromise that occurs. If defects occur primarily in the polymorphonuclear series, major difficulties could be encountered with common bacteria such as *Staphylococcus aureus*. If defects occur primarily in lymphocytes, infections caused by viruses and fungi could be more prevalent.

Although some consideration must be given to the possibility of complicated infections based on altered immunity, we shouldn't ignore what has already been found. Clinically important alterations in immune function have not occurred in the space program to this point. The types of infections that have been reported are simple, straightforward illnesses common to healthy adults readily diagnosed and treated by simple means. So while I agree with the group that we should include the capability to recognize complicated problems, planning should center around diagnosis and treatment of the mundane.

A discussion of infections and organisms possible follows.

Eye infections, particularly conjunctivitis, may occur frequently. I would expect common pathogens including adenovirus, HSV, chlamydia, *Haemophilus influenzae*, pneumococcus, and *Pseudomonas aeruginosa*. The closed environment may affect the organisms seen at this site, but I don't see a need for detailed expertise in diagnosis.

I essentially agree with the list of upper respiratory tract illnesses and pathogens as provided to us by Dr. Pierson. These infections should be infrequently seen if the preflight quarantine and screening cultures are effective. Pharyngitis would ordinarily be caused by respiratory viruses (I assume Dr. Couch will provide a list), group A strep and (with some controversy) group C and G strep, mycoplasma, and chlamydia. On the space station, these organisms should not be big problems although the capability of identifying them should be present. I would be more concerned about Candida albicans and reactivated herpes simplex as major causes of oral disease. I do not think it likely that staph, Haemophilus, or Corynebacterium diphtheria are a risk for oral disease. Otitis media may be a common and recurring problem for individual crew members. I agree with the list of organisms provided but would add anaerobic bacteria including peptococcus, peptostreptococcus, Bacteroides spp., and Fusobacterium spp. Otitis externa may also be a common problem and would most likely be caused by staph, strep, Pseudomonas aeruginosa, and Aspergillus spp. It will be important to identify these latter organisms since they require different treatment than is otherwise given. Sinusitis may also be commonly encountered and would include the same list of pathogens as otitis media.

I expect pulmonary infections to be a major concern on the space station. With constant exposure to airborne organisms, the risk of aspiration associated with space sickness and vomiting, possible limitations in immune responses, body fluid shifts that may lead to some degree of pulmonary edema and inhibited mucous clearance, pneumonia is likely to occur. I agree with the list of proposed pathogens with the additions of Mycoplasma, Chlamydia, Legionella, common upper respiratory tract anaerobes, and respiratory viruses.

Gastrointestinal infections should occur infrequently with preflight cultures and crew isolation, but could still be a problem. Should such illness occur it could be devastating since these organisms could easily spread to all crew members. The threat is real since cultures from humans and animals who are carriers without clinical illness are often negative, and food could be contaminated despite everyone's best efforts at preparation and storage. A list of pathogens is necessarily long because of the large number of organisms now associated with gastroenteritis, and with the inclusion of crew members from multiple different countries. Salmonella, shigella, campylobacter, yersinia, entertoxigenic and enteropathogenic _E. coli_, _Vibrio cholera_, _parahemolyticus_, and _vulnificus_, Aeromonas, _Clostridium difficile_, Norwalk agent, Rotavirus, Cryptosporidium, _Entaemeba histolytica_, and giardia are all possible in this context. It may be, however, that a more likely cause of gastroenteritis will be the contamination of food or water with toxin producing strains of staph or clostridia resulting in food poisoning with vomiting instead of diarrhea. Adequate quidelines for storage, preparation, and disposal of food items should prevent this from occurring.

Hepatitis should not be a concern on the space station except for the possible occurrence of the transmission of non A non B disease from one crew member to another. Since there is no screening method now to identify individuals with this virus(es), we will not be able to guarantee that this disease will not occur.

Intraabdominal infections of other sorts will be unlikely but possible. Of major concern will be the possibility of generalized peritonitis or peritoneal abscess following some intraabdominal event--ruptured peptic ulcer, ruptured appendix, ruptured diverticulum, etc. Such infections will invariably be associated with a mixture of the gastrointestinal flora. The question is what that flora will be after some time in space. I assume it will include primarily enteric gram-negative organisms, anaerobes, and enterococcus. It may also include candida, pseudomonas, and other less common organisms if they predominate as the normal flora in crew members.

Urinary tract infections may occur frequently in female crew members especially if they are sexually active. Prostatitis may occur in male crew members, but I would not expect this often. I agree with the set of pathogens already suggested for this site.

Sexually transmitted diseases should not be seen often if at all with effective preflight screening. The one exception would be genital herpes because of reactivation during the mission. I doubt that gonorrhea will occur. Chlamydia could be sexually transmitted, but I would be more worried about Chlamydia as a cause of pulmonary or eye disease.

Vaginitis, on the other hand may be an important problem.

Vaginal candidiasis, bacterial vaginosis, HSV, and vaginally associated toxic shock syndrome may be seen. Trichomonas should be eliminated by preflight examinations.

We discussed possible skin infections including abscesses, cellulitis, folliculitis, superficial mycoses, and superficial wound infections. Likely pathogens include staph aureus, group A strep, other streptococci, diphtheria, enteric gram-negative bacilli, pseudomonas, and candida. There would also be the risk of contamination of wounds from the plants and animals being used in experiments. Most of these plant and animal organisms will be similar to those seen ordinarily, but they may also include bacteria, viruses, and fungi not usually considered. Examples include leptospira, streptobacillus, and spirillium and a whole list of saprophytic fungi.

Bacteremia may occur and will most likely be secondary to infection at some other site, like pneumonia or urinary tract infection. It may also be a common complication of intravenous catheters since the numbers of organisms on the skin may increase and include more pathogenic bacteria than are normally seen in hospitals. I basically agree with the list of possible pathogens in Dr. Pierson's document.

Finally, central nervous system infections seem very unlikely in the group of people who will be on the space station, but certainly could occur. In addition to the bacterial causes listed, I would again add leptospirosis with the possible animal exposure. Aseptic, or viral meningitis may also occur, and in fact would be more likely in this age group. Brain abscess, or parameningeal infection may also represent more of a problem than bacterial meningitis given the strong possibility that individuals will have otitis media and/or sinusitis. Such superficial infections which may be difficult to recognize early could certainly be complicated by spread to the meningeal space. Organisms associated with brain abscess would then be more like those previously listed for otitis and sinusitis.

To summarize, the spectrum of diseases and organisms include a wide variety of possibilities. Our ability to predict those most likely is hampered at this stage by a lack of understanding of the immune status of individuals in space for prolonged periods of time, and knowledge of what will happen environmentally on the station after months to years without decontamination. Based on past experience, it appears that common minor ailments of healthy adults will be most common, but we also have to plan for possible major illnesses affecting crew members either individually or as a whole. I would plan most resources to cover skin, upper respiratory, urinary tract, and vaginal infections. If this is in fact the case, very little laboratory support will be required to deal with most clinical situations.

<u>2. Diagnostic methods</u>. I believe that the level of sophistication of the HCF for the diagnosis of the vast majority of clinical infectious diseases will not need to be that of a tertiary hospital. On the other hand, we can not clearly predict the nature of

the occasional devastating illness that may occur. This plus the need for continuing evaluation of the environment in the station suggest that the capability for very sophisticated diagnosis should be available. We probably do need the capability of identifying viruses, parasites, fungi, and sexually transmitted diseases. I would leave the decision for how to approach the diagnosis of viruses to Dr. Couch. Fungi and parasites can generally be handled by the use of microscopic techniques without the need for other equipment. The range of bacteria that could be seen, on the other hand, is potentially much greater than we are used to seeing in healthy adults now. I agree with the desire to have instrumentation comparable to the Vitek available to recognize these bacteria. I don't think we need to specifically identify anaerobes since treatment of these organisms is generally based on clinical syndromes and sites of infections rather than their specific isolation in the laboratory.

I also agree with the comments of Dr. Kass that by 1992 DNA probes may be extremely useful tools for diagnosis. I doubt that by that time they will be able to totally replace a traditionally based diagnostic system. I think we can assume that both methods will be important, and that neither can be used exclusively.

Equally important is the assumption in all of our discussions that images could be transmitted to an expert on the ground who would be in a position to aid in diagnosis. It is clear from studies of new instruments that inexperience can totally negate the expected utility of such devices. Recent studies on the use of strep identification kits in doctor's offices, for example, suggest that results may be wrong 50% of the time. Without ground control of the procedures being carried out, the results could be inaccurate and potentially harmful. For this reason inclusion of the digital imaging system being designed is absolutely essential.

I believe the Vitek is the best of the currently available automated systems for consideration in this context. It does have a couple of limitations. First, it will still require primary cultures for the growth of isolated colonies that can be used in identification procedures. Second, none of the automated systems is currently acceptable for the recognition of methicillin resistant staph. The first problem can not be eliminated, but can be minimized by the use of algorhythms for diagnosis that don't require cultures, and by using rapid tests directly from clinical material such as from throat swabs when possible. Specific DNA probes may be invaluable in selected situations to avoid the need for cultures. The second problem may be solved by improvements from Vitek or by simply including a selective agar medium containing methicillin that is sensitive enough to detect resistance.

Since many infections will be common, minor conditions, they will not require use of any instrumentation. The algorhythms for diagnosis as presented by Dr. Pierson begin with the collection of a specimen. I think that they should really start with a set of questions about the illness followed by the empirical approach to diagnosis and treatment before entering a mode that involves specimen collection and use of the laboratory. From our discussions I believe someone is already developing such algorhythms, and I will not expand further.

In addition most superficial infections should not be approached with extensive culture workups. Superficial cultures will invariably be contaminated with colonizing organisms. These organisms can not be defined as the cause of infection without evidence that they are invading tissue. In most situations on the space station such evidence will be impossible to obtain. Simply identifying bacteria or fungi from easily obtained cultures may be more harm than good if this identification leads to use of antibiotics to treat organisms that have nothing to do with clinical disease.

I would like to comment on the individual flow charts provided by Dr. Pierson.

Ear swab. Unless looking specifically for a fungus like aspergillus, or Pseudomonas aeruginosa, ear swabs will be of little value since the organisms isolated from a swab inserted in the external canal do not correlation with organisms causing otitis media. I would use an algorhythm for diagnosis and empirical treatment unless invasive disease is suspected. Then I would limit the workup to a single agar plate to look for fungi and one that will selecively grow pseudomonas. The fungi could ultimately be diagnosed by having a ground expert look at colony morphology and the microscopic structure of the hyphae. Pseudomonas could be identified by its appearance on the selective medium. Susceptibilities on the pseudomonas would be required using the Vitek.

Nose. I also consider swab cultures from someone's nose of little clinical value. It may be important to attempt to isolate respiratory tract viruses if they can be selectively treated. Studies comparing nasal swabs and direct aspirations of sinus cavities have shown that nasal swabs are a waste of time in identifying agents responsible for sinusitis. The only potential use for nasal swabs in bacterial identification would then be for periodic epidemiologic surveys of the crew. Unless such surveys will be done, I would not consider using this flow chart.

Throat swab. I think we could safely eliminate the culture arm of this chart and use only a rapid test--slide agglutination or flourescent antibody--for the identification of strep. We need to add, however, an arm for the recognition of candida, mycoplasma, chlamydia, and perhaps respiratory viruses. Candida could be identified by microscopic examination of a mouth scraping, mycoplasma and chlamydia by fluorescent antibody. I'm not sure at this stage how I would handle viruses from this site.

Phlegm producing cough. As discussed at the conference, sputum is a terrible sample under the best of circumstances in clinical laboratories. We will need to be able to evaluate sputum samples by microscopy on the ground to determine their relative value. We also need to be creative in using alternative methods, like latex agglutination of serum and urine, blood cultures, or DNA probes of sputum specimens for the diagnosis of pneumonia. In terms of the chart itself, I am reluctant to consider the use of a disks placed directly on primary isolation plates. I agree with studies that suggest that this is an insensitive way of identifying group A strep and pneumococcus. Again, we can identify both of these organisms by latex agglutination. The identification of staph aureus could be handled either by the Vitek or by latex agglutination also. The Vitek would be handy for the identification and susceptibility testing of the gram negative organisms grown on MacConkey. Other organisms that we included as potential causes of pneumonia will also require inclusion. Legionella can hopefully be handled by a direct fluorescent antibody, and chlamydia, mycoplasma, and the respiratory viruses as noted above. Fungal pneumonias and allergic pneumonitis, if they occur, will require invasive techniques like bronchial biopsy or pulmonary lavage for diagnosis.

Surface wounds. As with nasal cultures, swabs of the surface of open wounds could yield tragically misleading results. It is very difficult to separate colonizing flora from invasive pathogens. In my own lab I request physicians to obtain either deep tissue biopsies of the wound or aspirates of fluid through uninvolved skin at the margins. We should perhaps have a protocol for guiding personnel on the station in how to obtain such specimens. If such were available, I would agree with the flow chart as presented. If we will be limited to swab specimens, I would suggest that the workup of the culture be stopped before identification procedures if the culture grows more than one organism.

Gastrointestinal tract. I agree with the flow chart, but would add an additional agar plate for campylobacter, and have the materials available for the other pathogens I mentioned as potential causes of disease. I think the Vitek will be important in separating pathogenic organisms from the normal flora. I would also hope that DNA probes will be available by then that could be used directly on the fecal specimen. That would be a real plus in avoiding the complex methodology necessary now.

Urinary tract infections. I agree with the flow chart as provided. Crew members, especially women, will need to instructions for specimen collection.

Vaginal sample. I agree with the flow chart except that I don't think that a culture plate is necessary for growth of yeasts. If yeast cells are not recognized on gram stain, their growth on an agar plate will probably not be meaningful in diagnosis. I assume that identification of staph is being considered in case of possible toxic shock syndrome. It is important to emphasize that this entity is best recognized clinically, and while cultures growing staph help confirm the diagnosis, growth or lack of growth of staph may not confirm or refute the presence of TSS.

CSF. I agree with the flow chart with the comments about A and P disks on primary plates as noted above. All of these primary organisms can be ultimately identified by the Vitek or latex agglutination. Other organisms we discussed as potential pathogens should grow on the plating media listed and could then be identified by the Vitek. The gram stain in this situation is vitally important, and again emphasizes the need for transmission of images to an expert on the ground for review.

Bacteremia. I have some difficulty deciding on the best system to use for the detection of bacteremia. It will certainly be important for the chosen system to be capable of detecting a variety of pathogens including common bacteria and fungi. No single system now in use is perfect for the detection of all the possible organisms we are considering. Given the space and weight limitations in the HCF, I would suggest use of the DuPont lysis centrifugation system. This would require a small centrifuge (something you'll need anyway), and the tubes for blood drawing. Once centrifuged, cultures would then be set up on agar media already available. This system would avoid the need to carry prepared blood culture media, something that would otherwise be necessary. It is a very good system for the recognition and identification of most bacteria, and is the premiere system now marketed for the growth of fungi. It's disadvantages are that it doesn't do well for anaerobes (something we've already decided to sidestep), and it is somewhat more likely to grow contaminants than other methods. I think both of these problems are fair trades for the ease of use and capability the system has in other areas.

My flow chart for bacteremia would therefore be somewhat different. I would start with inoculation of a lysis tube, then plating of supernatent onto a blood-chocolate-MacConkey triplate, and a sabouraud plate, and proceed from there.

Other possible sites. There is no flow chart for eye cultures. I would create one that would again start with a clinical algorhythm, then include selective cultures for adenovirus, *Haemophilus influenzae*, pneumoncoccus, and *Pseudomonas aeruginosa*.

There is also no chart for skin cultures apart from wounds. My comments about cultures for wounds apply here also in that cultures will often be misleading because of the colonizing flora. On the other hand, skin scrapings for microscopic examination to look for fungi will undoubtedly be important.

A variety of infections can be diagnosed by serologic means, and the capability for this approach should be in place. Examples where this approach is now important include EB virus, hepatitis, CMV, influenza, Legionella, typhoid fever, brucellosis, leptospirosis, and toxoplasmosis. By 1992 there may be genetic probes capable of detecting a variety of common organisms using serum samples with the elimination of the cultural methods needed now.

3. Procedures for Minimizing Disease.

The preflight protocol for crew members will be most important for the prevention of disease after lift off. As we discussed, the preflight quarantine should be a rigid 14 days with the qualifications for longer periods if family considerations dictate. Screening cultures should include urethral and cervical samples. A preflight serum should be available for a battery of tests should the situation in space dictate--these should include tests for the invasive fungi, CMV, toxoplasma, the rickettsia, syphilis, Legionella, mycoplasma, and chlamydia. Some of these tests are important to include because of the exposure to plants and animals that will occur on the station. Dr. Smith's suggestion to screen all individuals for antibody to the toxic shock toxin is also excellent.

On the other hand, preflight bacterologic screening needs to be limited to some predefined extent. It sounds good to say that all potential pathogens isolated in preflight cultures will be identified, and tested for antimicrobial susceptibility, but in reality such a venture would be extremely complicated. Everyone is colonized with organisms that could be considered potential pathogens. The particular organisms will vary from one person to another, and the recognition that they exist is in large part a reflection of the effort expended. For example, to be sure that someone is not harboring a toxigenic strain of _E. coli_ one must completely workup 20-30 individual colonies from each primary isolation plate. Twenty to thirty colonies of staphylococcus from each plate would need to be examined for possible resistance to methicillin. The point is that preflight screening will be somewhat reassuring, but will not definitely prevent the occurrence of the disease one would like to avoid in space. I don't think that a great deal of time should spent on the evaluation of these cultures. I am in favor of a limited, defined protocol to look for a small list of organisms that we have the means of eliminating before the flight. Examples include salmonella, shigella, campylobacter, tuberculosis, meningococcus, group A strep, ameba and giardia.

I would accept a protocol for biotyping selected isolates preflight providing the same biotyping system is available on the station. Either Vitek identification or DNA amnalysis have the potential to allow for useful characterization of isolates. Such information could be very useful should an epidemic of infections occur.

I agree with the concept addressed in appendix 1 that preflight immune status for certain pathogens should be known. I would add to the list the potential for preflight serologies to fungal pathogens including cocci, histo, and blaso. As we gather more information about the immunologic consequences of prolonged space flight, these may be very important. Apparently there has not been a decision to mandate vaccinations against common pathogens before flight. As we discussed, vaccinations for influenza, Herpes zoster, CMV, pneumococcus, Haemophilus influenzae, and meningococcus should be required. By 1992 additional vaccines may also be available that could be valuable for the crew members.

Even though we are not mandated to address environmental topics, it should be emphasized by our group as well as others that careful monitering of plants, animals, air, food, and water before shipment to the space station are vitally important in the prevention of diseases among crew members and can effectively limit the spectrum of infectious disease agents that will be seen.

We were asked to provide a list of antimicrobial agents that will be needed. The main point to make is that antimicrobial agents are changing so rapidly that to provide anything other than a class list of agents would be meaningless. Given that most of the infections expected will be minor, the most needed will be a set of oral antibiotics, probably penicillin or ampicillin, a cephalosporin, erythromycin, sulfa-trimethoprim, metronidazole, acyclovir, and amantidine. For the rare serious infection a set of powders for reconstition and parenteral administration will also be needed. A list of such agents should include an antistaphylococcal penicillin, an antipseudomonal penicillin, a third (fourth?) generation cephalosporin, an aminoglycoside, erythromycin, vancomycin, a quinolone, amphotericin B, and acyclovir. There should be 2 or 3 empty slots saved for new drugs that will also likely be considered important at that time.

A related topic that falls into the category of disease control is rigid control of the antimicrobials being dispensed. We were reassured at the conference that access to the drug cabinet would be strictly controlled. That is important. Equally important, but not discussed, is the manner in which drugs are utilized. It should be emphasized that none of the antimicrobials be dispensed beyond a defined, limited time without ground approval for their continuation. It is also important to again emphasize the need for appropriate laboratory information on which to base treatment decisions. Poorly collected, superficial wound cultures, inadequate sputum specimens, and inadequately controlled rapid tests will lead to inappropriate identification of organisms and meaningless susceptibility testing. The real danger from such results is over utilization of unnecessary antimicrobials. Over prolonged periods, such use of antibiotics would undoubtedly lead to the development of resistant strains of bacteria that will be more difficult if not impossible to treat with available drugs.

A critical question is how many infections to expect since the number of supplies, drugs, reagents, and space will be dependent on such a prediction. I imagine that there will be a need for 5-10 courses of oral antibiotics for each mission and that ordinarily no parenteral agent will be used. Major illnesses will be of two types--those limited to the individual primarily infected as would happen with a ruptured viscous and peritonitis, and those that become epidemic as with some of the respiratory and gastrointestinal diseases possible. Should an epidemic occur, it could affect the entire crew. This implies that enough of each antimicrobial agent must be available to treat as many infections as there are crew members.

4. Studies needed now. I think the unanswered, vital issues to be addressed before the space station deployment were adequately

listed as 7 separate items by Dr. Couch. I would again emphasize two of these: the need for immunological studies, and the need to evaluate the proposed methodologies under the operating conditions of space.

As mentioned, specific, objective information about the frequency of reactivated herpes infections, oral candidiasis, and gingivitis from past missions would provide helpful clues now in assessing immune status. It is also essential at this point to carry out studies of every phase of the immune response under actual space conditions.

It is also essential that all possible methodologies being considered for diagnostic use be tested under actual operating conditions in space. We must know if bacteria grow normally, have the same microscopic and colonial morphology, react the same way biochemically in the Vitek, and give the same results for sensitivity testing. We must know if latex agglutination, fluorescent antibody staining, genetic analysis, etc. will work. The way to find this out is simple: perform all of the quality control tests routinely performed in clinical laboratories with control strain organisms for <u>all</u> tests being considered on one or more of the shuttle missions. Results of such tests may totally revise our thinking about the best diagnostic system to have available.

Something we did not discuss is a protocol for preflight training of crew members. I assume NASA has well developed methods for preflight training in general. We need to be sure that crew members understand the algorhythms developed for diagnosis and treatment, and they need to be familiar with the use of the equipment that is present on the station. Someone needs to design the training course for the crew to meet these goals.

Most of this letter has been a regurgitation of the discussion at the meeting. I hope, however, that I have brought out a few points that were not extensively discussed, especially concerning methodology. If you need more information at this time let me know.

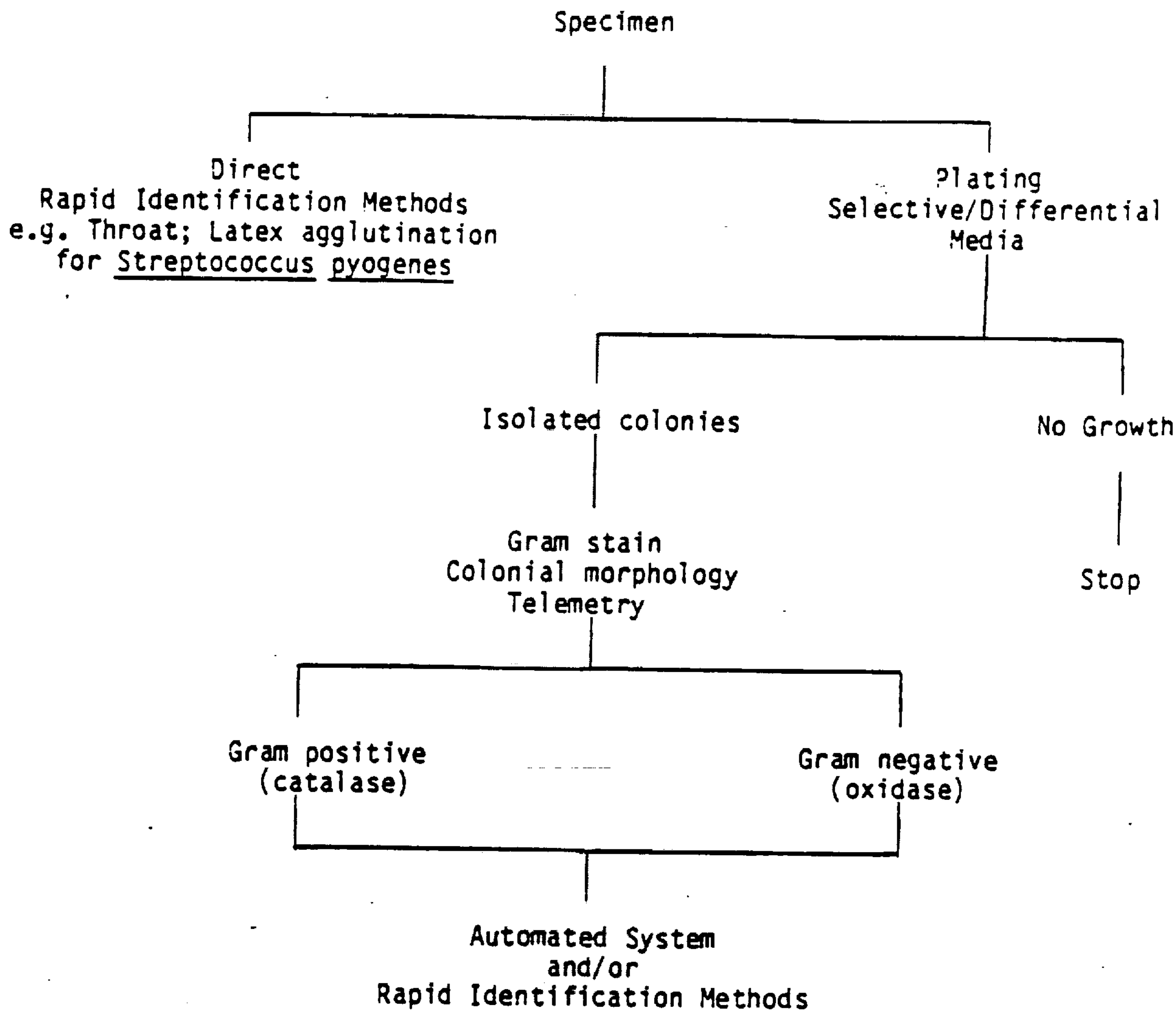
I would also like to offer my services to help in the design of the preflight training course for the crew, clinical and laboratory algorhythms, refinement of the technical diagnostic procedures being discussed, and protocols for pre-space station evaluation of methodologies. We have previously offered the facilities of the University of Utah for design and field testing of the microbiological package for the HCF. Our offer still stands.

Sincerely,

Larry G. Reimer, M.D.
Director, Clinical Microbiology
VAMC, Salt Lake

APPENDIX B

MATERIALS SUPPLIED TO PARTICIPANTS


Specimen
Direct
Rapid Identification Methods
e.g. Throat; Latex agglutination
for Streptococcus pyogenes
Plating
Selective/Differential
Media
Isolated colonies
No Growth
Stop
Gram stain
Colonial morphology
Telemetry
Gram positive
(catalase)
Gram negative
(oxidase)
Automated System
and/or
Rapid Identification Methods

PROPOSED MICROBIOLOGICAL SUPPORT

PLAN FOR SPACE STATION

PREFLIGHT

Days Prior To Flight	Activity
90	• Review of crewmembers' immune status to selected infectious agents (See Appendix 1)
30	• Flight Physical (Crew Physician) includes complete clinical chemistry workup (See Appendix 2)
	• Microbiological analysis of crewmembers Include: Ears, nose, throat, skin, urine, feces, sputum, blood (Hepatitis A&B and RPR)
14	• Quarantine
	• Microbiological analysis of crewmembers (same as F-30 except one additional throat swab will be taken for viral isolation) (See Appendix 3).
10	• Flight Physical (Same as at F-30)
7	• Microbiological analysis of crewmembers (Same as F-14)
1	• Flight Physical (No laboratory work)
	• Microbiological analysis of crewmembers (Same as F-14)

- Antibiotic susceptibilities will be determined for all potential bacteriological pathogens isolated during preflight microbiological evaluations.
- Bio-typing of selected isolates (e.g., phase typing of *Staphylococcus aureus*) will be conducted for epidemiological applications.
- Preflight microbial monitoring of the Space Station environment (Air, surfaces, water, and food) will be conducted to ensure a safe environment for crewmembers (see Microbiology Requirements and Specifications for Space Station Document)

INFLIGHT

Inflight diagnostic microbiological capability will reside in the Health Maintenance Facility (HMF). Inflight sampling will occur only when indicated; no routine sampling is planned.

CAPABILITIES

- Culture collection
- Isolation of pure cultures
- Gram staining apparatus
- Identify wide range of aerobic and microaerophilic pathogens
- Determine antibiotic susceptibilities
- Yeast identification (germ tube)
- Storage/transport equipment and media
- Biohazard containment and disinfection

EQUIPMENT (Major)

- Refrigerator/Freezer
- Incubator
- Microscope with telemetry
- Glove box
- Auto Microbic System (Incubator/Reader only)

TABLE 1. MICROBIOLOGY DIAGNOSTIC CAPABILITY FOR HMF

SYSTEM CONTINGENCY	SPECIMEN	ASSOCIATED DISEASES	PATHOGENS	SPACE STATION CAPABILITY	DIAGNOSTIC APPROACH
Upper Respiratory Tract	Throat Nose	Pharyngitis Common Cold Nasopharngngitis	*Streptococcus* Group A *Candida albicans* Respiratory viruses *Corynebacterium diptheriae* *Staphylococcus aureus* *Haemophilus influenzae*	*Streptococcus pyogenes* *S. pneumoniae* *C. albicans* *S. aureus* *H. influenzae*	Latex agglutination and AMS Direct plating on blood with A disc Isocult/Throat Streptococcus
	Ear	Otitis media	Middle ear *Streptococcus pneumoniae* Group A *Streptococcus* *Staphylococcus aureus*	All pathogens	Direct plating on Triplate containing Blood agar, Baird-Parker, MacConkey, Latex Agglutination or AMS
	Sputum	Bacterial pneumoniae	*Streptococcus pneumoniae* *Haemophilus influenzae* *Staphylococcus aureus* Gram-negative enteric bacillus and *P. aeruginosa*	All pathogens	Direct plating onto Blood agar and Biplate containing Baird-Parker and MacConkey. Latex Agglutination Gram Stain

TABLE 1. MICROBIOLOGY DIAGNOSTIC CAPABILITY FOR HMF

SYSTEM CONTINGENCY	SPECIMEN	ASSOCIATED DISEASES	PATHOGENS	SPACE STATION CAPABILITY	DIAGNOSTIC APPROACH
Gastro-intestinal Tract	Feces	Salmonellosis Shigellosis	Salmonella sp. Shigella sp. Yersenia enterocolitica Campylobacter jejuni E. coli (enterotoxigenic)	Salmonella sp. Shigella sp.	Direct plating on triplate contain- MacConkey, Hektoen, Bismuth Sulfate, GN Broth Isolated colonies to Enterotube II or AMS
Genitourinary Tract	Urine	Pyelonephritis Urethritis	E. coli Klebsiella sp. Enterobacter sp. Proteus sp. Other enteric G-R and Pseudomonas aeruginosa Enterococci Staphylococcus aureus Candida albicans	All pathogens	Urine paddle Enterotube II Oxiferm tube or AMS
	Vagina	Candidiasis	Trichomonas vaginalis Candida albicans Haemophilus vaginalis Gonococcus Herpes simplex (type II) Enteric G-R Streptococcus pyogenes Staphylococcus aureus	Trichomonas vaginalis Candida albicans Staphylococcus aureus Streptococcus pyogenes	Microscopic wet mounts and Gram stain Direct plating to Biplate containing Sabouraud, Baird Parker. Isocult Candida/T. vaginalis

TABLE 1. MICROBIOLOGY DIAGNOSTIC CAPABILITY FOR HMF

SYSTEM CONTINGENCY	SPECIMEN	ASSOCIATED DISEASES	PATHOGENS	SPACE STATION CAPABILITY	DIAGNOSTIC APPROACH
Circulatory System	Blood	Bacteremia	Staphylococcus aureus Staphylococcus epidermidis E. coli Klebsiella sp Enterobacter sp P. aeruginosa Proteus spp. L. monocytogenes Anaerobes, Bacteroides spp., and Clostridium spp. Candida albicans	All pathogens except anaerobes Bacteroides spp. Clostridium spp.	Gram stain Direct plating to triplate containing Blood, and MacConkey. Isolated colonies Gram stain Coagulase Enterotube II Oxiferm tube or AMS
Central Nervous System	CSF	Bacterial Meningitis	Haemophilus influenzae Nisseria menigitidis E. coli, other G-R and P. aeruginosa, Staphylococcus aureus Streptococcus sp Cryptococcus neoformans Candida albicans Listeria monocytogenes	All pathogens	Direct plating to triplate containing chocolate, Blood agar, MacConkey Isolated colonies Gram stain Enterotube II Oxiferm tube Directogen Latex Agglutination or Phadebact Coagglutination or AMS
	Wound	Bacterial Cellulitis Gas gangrene (myonecrosis)	Staphylococcus aureus Streptococcus pyogenes Anaerobic Bacteria Enterobacteriaceae P. aeruginosa Enterococci	S. aureus S. pyogenes Enterobacteriaceae P. aeruginosa Enterococci	Direct plating on triplate containing Blood, Baird-Parker and MacConkey. Isolated colonies Gram stain Coagulase Enterotube Oxiferm tube or AMS

INFLIGHT DIAGNOSTIC APPROACH

1st Choice - Auto Microbic System (Automated)

- Advantages
    - Established Technology
    - Minimum Crew Time
- Disadvantages
    - Weight
    - Down Time

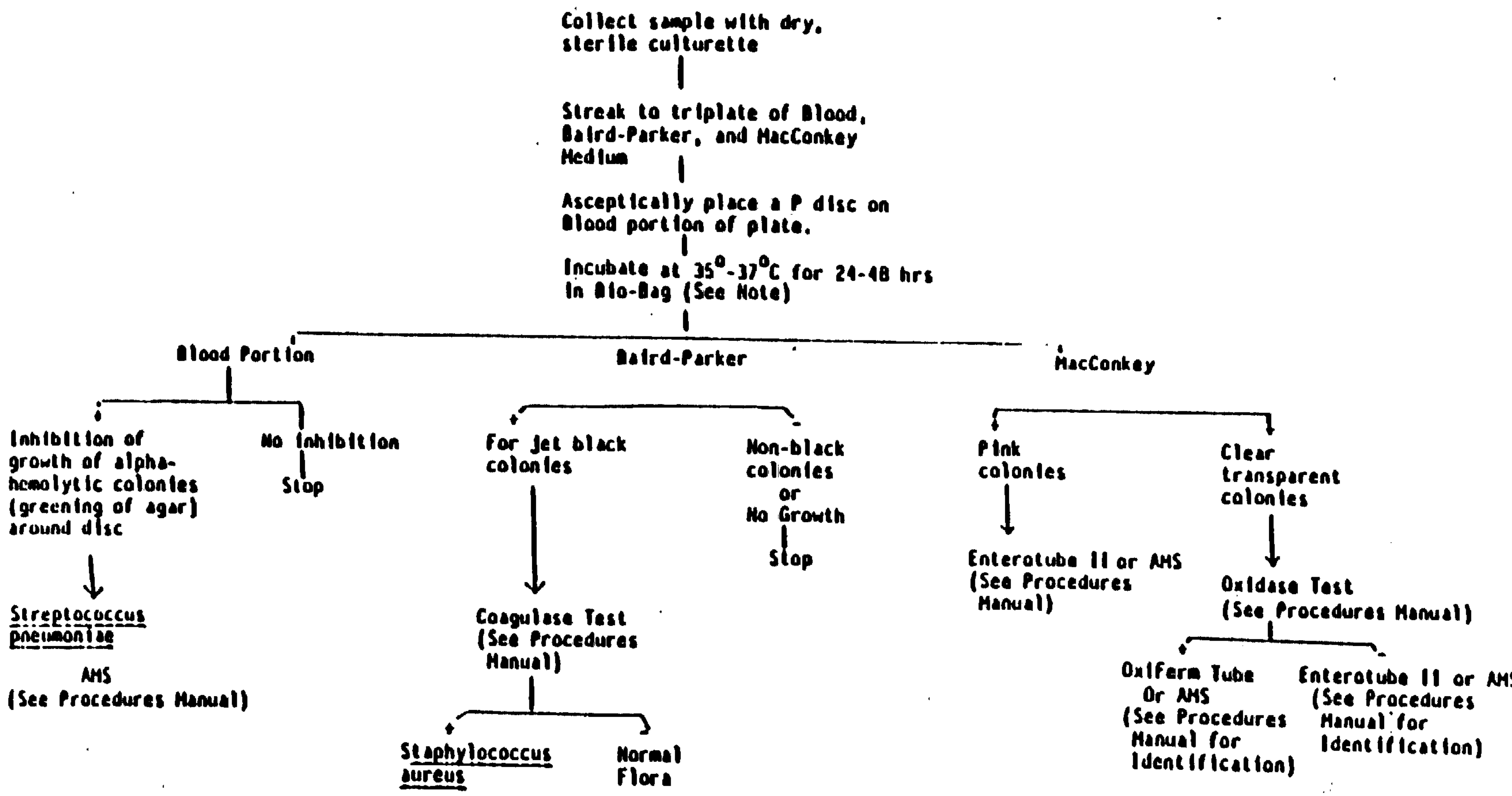
2nd Choice - Auto Microbic System (Manual)

- Advantages
    - Established Technology
- Disadvantages
    - Increased Crew Time
    - Requires Increased Time

3rd Choice - Diagnostic Kits

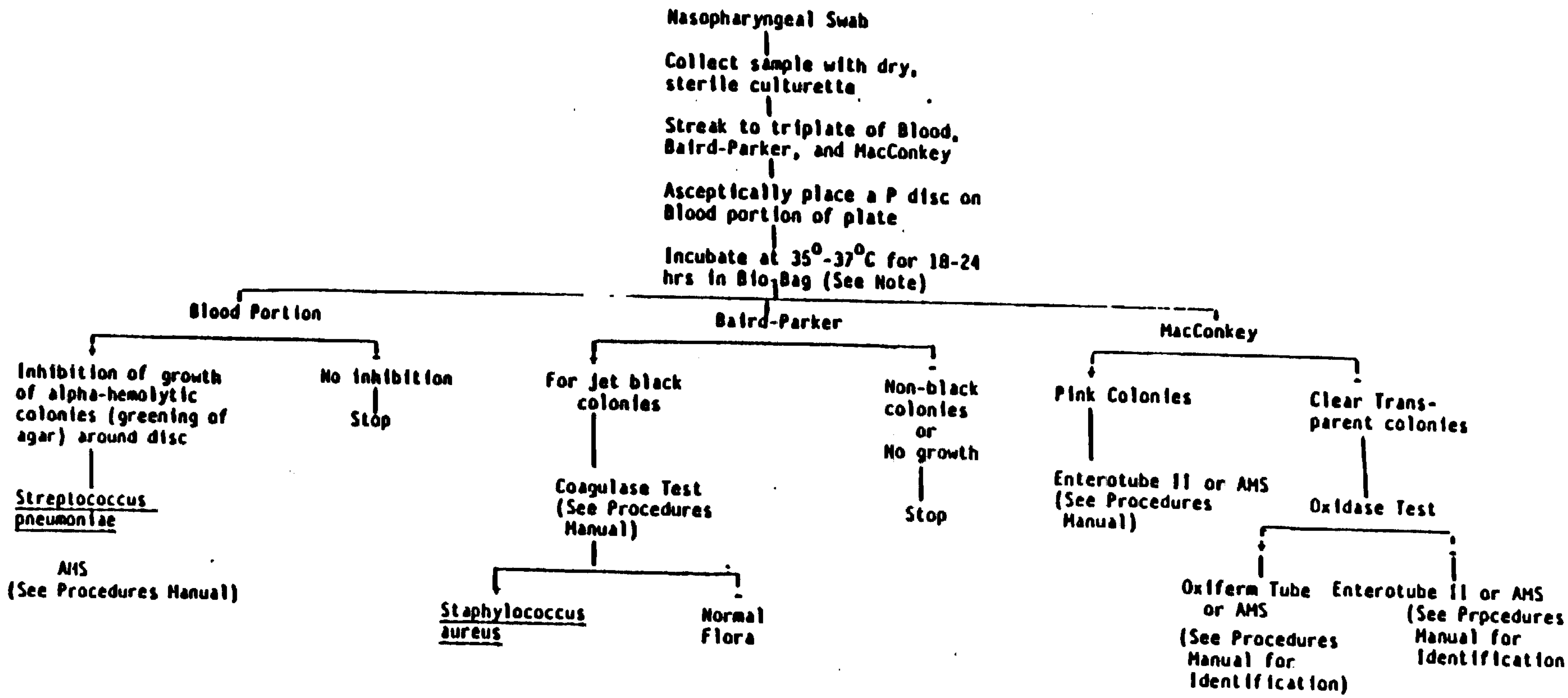
- Advantages
    - Flexible
- Disadvantages
    - Increased Crew Time

EAR SWAB



NOTE: If slight or no growth at 18-14 hrs, reincubate an additional 24 hrs.

NOSE



NOTE: If slight or no growth at 18-24 hrs, reincubate an additional 24 hrs.

THROAT SWAB

Swab throat
Avoid teeth and tongue
Use depressor if necessary

Two Swabs

Swab and Streak BA
Stab Medium and Place
"A" disc asceptically
on agar
Incubate in-Bio-Bags at
35°-37°C for 18-24 hrs
(See Note)

Growth around
"A" disc; no Beta
hemolysis

Normal Flora

No growth around
"A" disc; Beta hemo-
lytic colonies (clear-
ing of blood)

Gram stain
+ cocci; pairs and
chains

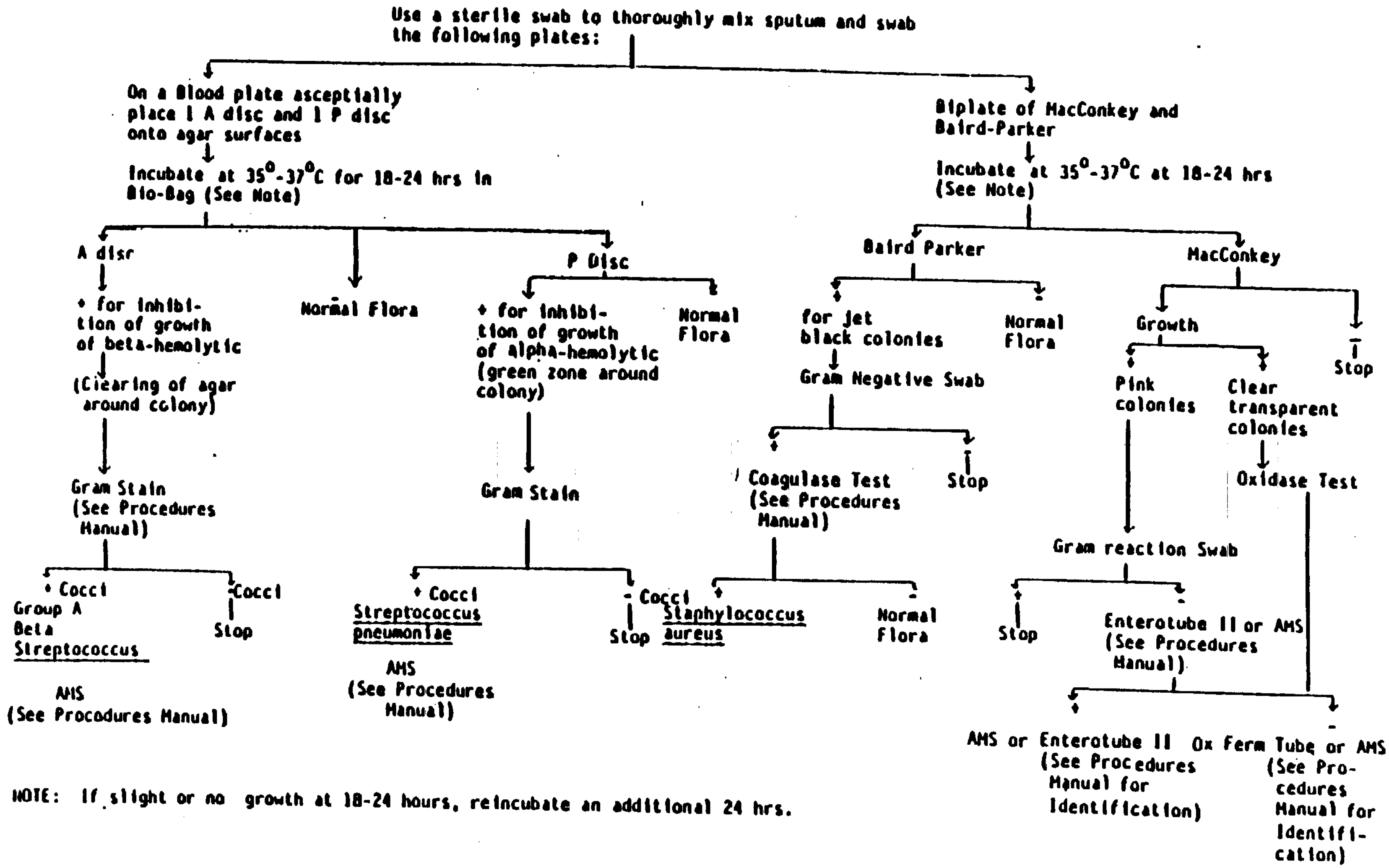
AMS (See Procedures Manual)

Group A Beta Steptococcus

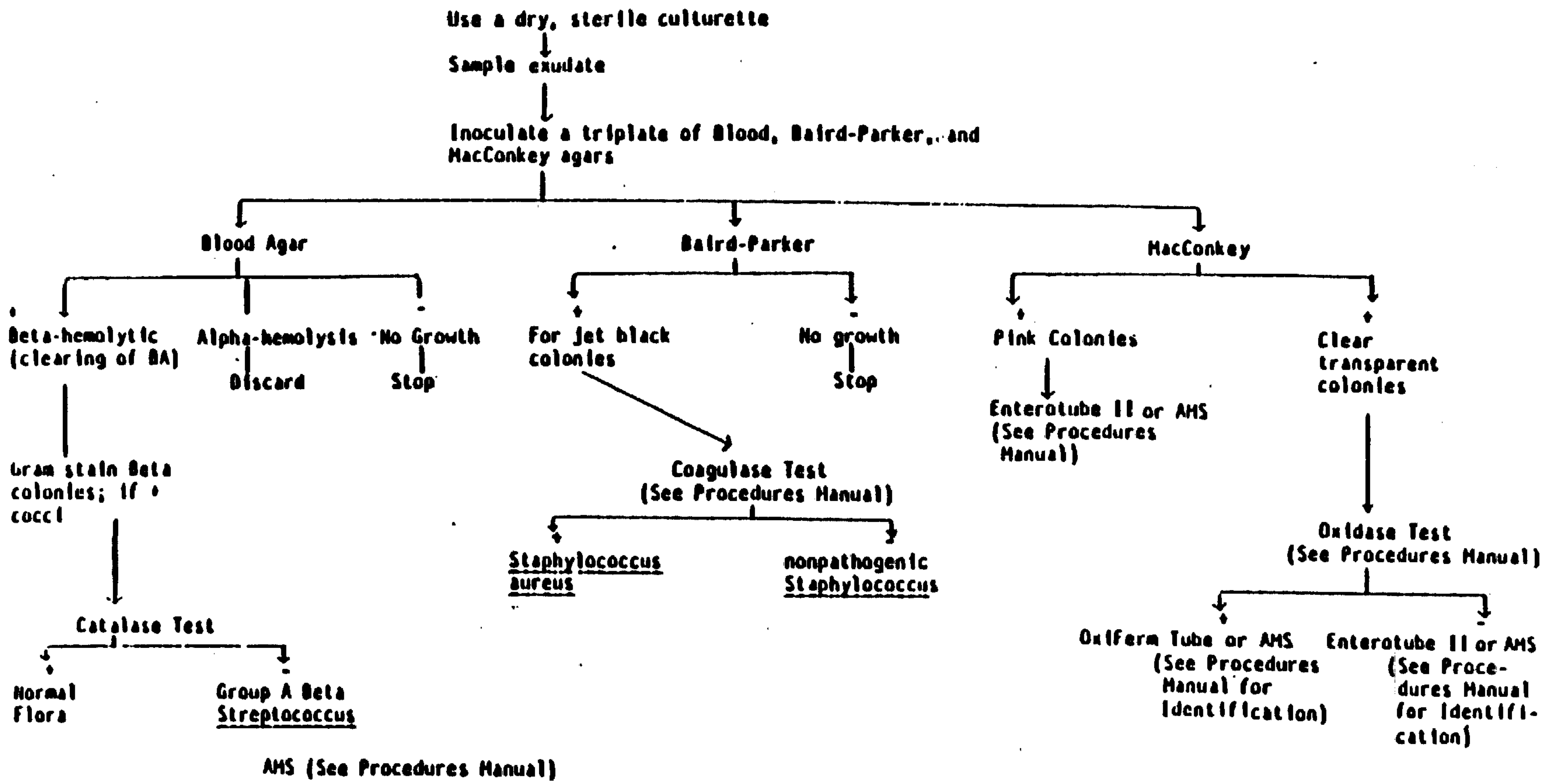
Latex Slide
agglutination
for detection
of Group A
streptococcal
antigen

See procedure
manual for
detailed
instruction

NOTE: If slight or no growth at 18-24 hours, reincubate an additional 24 hrs.

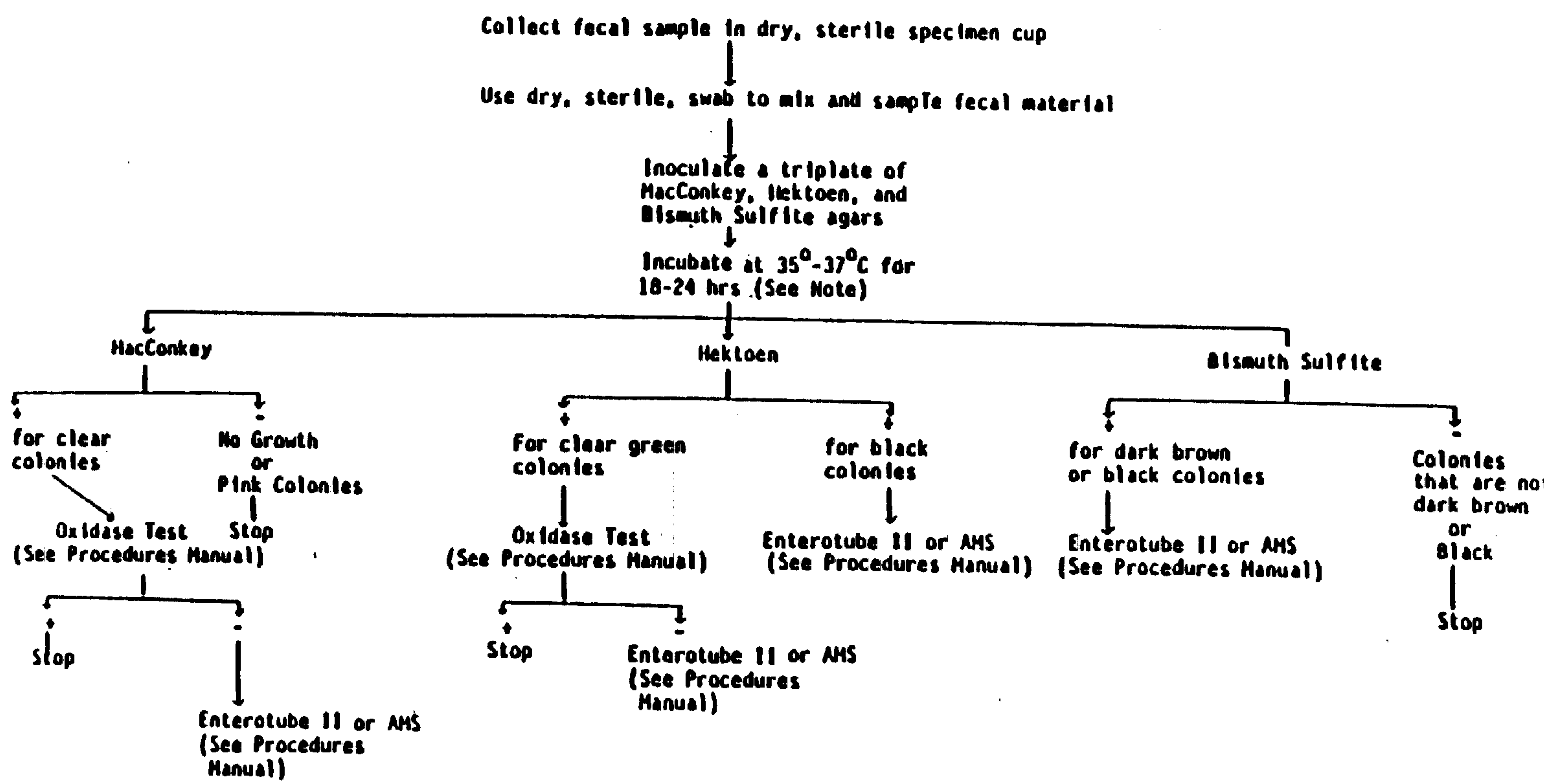


NOTE: If slight or no growth at 18-24 hours, reincubate an additional 24 hrs.



NOTE: If slight or no growth at 18-24 hrs, reincubate an additional 24 hrs.

GASTROINTESTINAL TRACT



NOTE: If slight or no growth at 18-24 hrs, reincubate for an additional 24 hrs.

URINARY TRACT INFECTIONS

A clean-voided midstream
(first void) urine directly
on to Urine Paddle containing

MacConkey and Cled Media

↓

Place paddle into container
Incubate 18-24 hrs 35^{o}-37^{o}C

↓

Compare to density chart
for bacterial concentration

MacConkey

Clear transparent
pink Oxidase

↓

Enterotube II

Clear transparent
Oxidase +

↓

OxiFerm Tube

↓

Inoculation and Identification
in Procuedures Manual

Cled

Catalase

AMS (See Procedures Manual)

+
Staphylococcus

-
Streptococci

VAGINAL SAMPLE

- Two dry, sterile Culturette Swabs used to sample vaginal area
  - Swab #1
    - Swab will be rolled over two clean glass slides
      - Slide #1
        - Gram Stain
          - Look for presence of Gram and budding yeast cells
      - Slide #2
        - Wet Mount
          - Look for presence of budding yeast cells and/or *Trichomonas* Trophozoites
  - Swab #2
    - Inoculated onto a biplate containing Baird-Parker and Sabouraud media. Incubate 35^{o}-37^{o}C for 48 hrs
      - Baird-Parker
        - + Black colonies with clearing around colonies
          - Coagulase
            - + : *Staphylococcus aureus*
            - - : Normal Flora
      - Sabouraud
        - Examine plate. If no growth is present, reincubate an additional 24 hrs. Reexamine plates. If colony formation is present on the Sabouraud medium, make an isolation streak onto a plate containing Sabouraud medium. Incubate for 24 hours. Identify according to Uni-Yeast-Tek Yeast Identificatio system or AMS to be found in Procedures Manual.

CSF

Collect spinal fluid in sterile container

Gram Stain

Streak to Biplate Blood and Chocolate

- Blood Agar + A & P discs
  Place in Bio-Bag and incubate at 35^{o}-37^{o}C for 24-48 hrs
  - Beta hemolysis (Clearing of Blood) No growth around A disc
    - Catalase Negative
      - <u>Streptococcus Pyogenes</u>

        AMS (See Procedures Manual)
    - Catalase Positive
      - <u>Staphylococcus epidermidis</u>

        or

        Coagulase Positive
        - <u>Staphylococcus aureus</u>
  - Alpha hemolysis
    - (green zone around colonies) No growth around P disc
      - <u>Streptococcus pneumoniae</u>

        AMS Procedure (See Procedures Manual)
- Chocolate
  Place in Bio-Bag and incubate at 35^{o}C-37^{o}C for 24-48 hrs
  - Oxidase Test
    - + <u>Neisseria menigitidis</u>
      - *Latex Agglutination or AMS
    - \- <u>Haemophilus influenzae</u>
      - *Latex Agglutination or AMS

*See Procedures Manual for instruction

BACTEREMIA

Blood
↓
3 or 4 cultures per day
at 1 hr intervals
↓
place

3 to 5 ml Blood
into
Vacuneda

Blood Culture
Bottle

Incubate 35^{o}-37^{o}C
for 14 days
↓
Check daily for growth
in bottle

If positive
↓
Draw out sample with syringe

and place on

Biplate containing
Chocolate Bacitracin
Blood agar + A disc
in Bio-Bag at
Incubate for 35^{o}-37^{o}C
for 24 - 48 hrs

Chocolate Bacitracin
↓
+ growth
Gram stain
↓
G-R (No growth on
↓ MacConkey)
Streak to TSA + XV, X
V-ring or AMS

Growth around
XV only

<u>Haemophilus</u>
<u>influenzae</u>

Blood Agar -
A disc
No growth
around A disc,
Beta Hemolysis
↓
Catalase Neg
<u>Streptococcus</u>
<u>Pyogenes</u>

Latex Aggluti-
nation or AMS
(See Procedures
Manual)

Triplate containing
Blood, Baird-Parker
McConkey
↓
Incubate at 35^{o}-37^{o}C
for 24 - 48 hrs.

Blood + P disc
↓
No growth
Green zone around colonies
↓
<u>Streptococcus</u> <u>pneumoniae</u>

Latex Agglutination (See Procedures
or Manual)
AMS

MacConkey

Pink or oxidase Negative
↓
Enterotube II
↓
See Procedures Manual

Oxidase positive
↓
Oxiferm Tube or AMS
↓
See Procedures
Manual

Baird-Parker
↓
Postive for black colonies
Clearing around colonies
↓
Coagulase +
↓
<u>Staphylococcus</u> <u>aureus</u>

POSTFLIGHT

Days Prior To Flight	Activity
0	• Microbiological analysis of the crewmembers. (Same as preflight F-14 exam)
7 (Optional)	• Same as Above

APPENDIX 1

Serology testing to determine crewmembers' immune status to following viral and bacterial agents:

- Hepatitis A and B
- Epstein - Barr
- Mumps
- Rubella
- Rubeola
- Varicella Zoster
- Cytomegalovirus

- Clostridium tetani (current immunization)
- Corynebactemium diptheriae (current immunization)
- Mycobacterium tuberculosis (current skin test)

APPENDIX 2

TABLE 1
BLOOD PARAMETERS - ASTRONAUT ANNUAL AND FLIGHT EXAMS

Hematology

RBC
Retic
Hct
Hgb
ZSR
Plat
MCV
MCH
MCHC
WBC
WBC Diff
Ferritin

Chemistry

Glu	Na
BUN	K
Uric Acid	Cl
Creat	PO_4
Bili. T.	Ca (T)
SGOT	Ca (Ion)
SGPT	Mg
Alk. Phos.	Osmol.
CPK	CO_2
LDH	Choles.
GGTP	Trig.
AMY	HDL

Serology

HAVAb
HbsAg
CRP
RPR

Immunology

T. Protein	IgG
Albumin	IgA
Alpha-1	IgM
Alpha-2	IgD
Beta	IgE
Gamma	Transferrin
Lipoprotein Alpha 1	Haptoglobin
Lipoprotein Pre-Beta	Alpha-2-Macroglobulin
Lipoprotein Beta	Alpha-1-Antitrypsin
LDH Isoenzyme	Properdin Factor B
CPK Isoenzyme	
C3	
C4	

Endocrinology

Cortisol
TSH
T3
T4
HGH
Insulin
Aldosterone
Angiotensin I

TABLE 2
URINE PARAMETERS - ASTRONAUT ANNUAL AND FLIGHT EXAMS

ROUTINE URINALYSIS

Chemistry (Qualitative)	Microscopic Exam
Nitrite	WBC
pH	RBC
Protein	Epithelial cells
Glucose	Mucus
Ketones	Casts
Urobilinogen	Crystals
Bilirubin	Bacteria
Blood	Parasites
Leukocytes	
Specific Gravity	
Color	
Appearance	

TABLE 3
24 HOUR URINE PARAMETERS - ASTRONAUT FLIGHT EXAMS

Chemistry	Endocrinology	Heavy Metals
Volume	Aldosterone	Arsenic
Specific Gravity	Cortisol	Cadmium
Osmolarity	Testosterone	Chromium
Na	Total Epinephrine	Lead
K	Total Norepinephrine	Mercury
Cl	ADH	
Ca		
Mg		
PO_4		
Uric Acid		
Creatinine		
Oxalate		
Citrate		

APPENDIX 3

Throat swab will be processed for the following viruses and mycoplasmas:

- Influenza
- Parainfluenza
- Herpes Simplex
- Adenoviruses
- Coxsackie
- Rhinovirus
- Enterovirus
- *Mycoplasma pneumoniae*
- *Mycoplasma hominis*

DISCUSSION QUESTIONS

- Do we need to define an inflight capability for the following microbial agents?

  Viruses

  Anaerobes

  Chlamydiae

  Filamentous Fungi

  Legionella

  Parasitology

- Should microbial procedures be carried out in a glove box?
- Is the Quarantine Period appropriate?
- Is a preflight venereal disease screening needed?
- What antibiotics should be included in the Health Maintenance Facility?
- Should crewmembers be vaccinated against specific infectious disease agents? Which ones?
- What additional capabilities and equipment are needed?